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MENINGIOMAS

ORIGIN, DIVERGENCE IN STRUCTURE AND RELATIONSHIP TO CONTIGUOUS TISSUES IN LIGHT OF PHYLOGENESIS AND ONTOGENESIS OF THE MENINGES, WITH SUGGESTION OF A SIMPLIFIED CLASSIFICATION OF MENINGEAL NEOPLASMS

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The probable origin and true histologic character of the meningioma, a tumor best known as dural endothelioma, are fairly old problems. A century ago, Cruveilhier [1] (1835) intimated the meningeal origin of such tumors by naming them "cancerous growths of the meninges." He substituted this name for the older term "fungus growth of the dura," used by earlier writers. Since then, almost each decade has brought to the foreground important contributions on this subject, embodying observations and conclusions of some outstanding anatomist, pathologist or neurosurgeon. At first sight it would seem that these studies have resulted in little more than the creation of a large assortment of names, which include such terms as cylindroma, of Billroth; [2] psammoma and dural sarcoma, of Virchow; [3] epithelial cancer, of Bennett; [4] fibroplastic tumor, of Lebert; [5] epithelioma, of Bouchard [6] and Robin; [7] endothelioma, of Golgi; [8] cancer of the arachnoid, of Rokitansky; [9] arachnoid fibro-

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1. Cruveilhier, J.: Anatomie pathologique du corps humain, Paris, J.-B. Baillière, 1835.

2. Billroth, C. A. T.: General Surgical Pathology and Therapeutics, translated by C. E. Hackley, New York, D. Appleton & Co., 1889.

3. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863.

4. Bennett, J. R., quoted by Cushing.[12]

5. Lebert, H.: Traité d'anatomie pathologique, générale et spéciale, Paris, J.-B. Baillière & fils, 1857-1861.

6. Bouchard, C. J.: Case Report, Bull. Soc. anat. de Paris **39**:21, 1864.

7. Robin, C.: Recherches anatomiques sur l'épithélioma des séreuses. J. de l'anat. et physiol. **6**:239, 1869.

8. Golgi, C.: Sulla struttura e sullo svilluppo degli psammomi, Morgagni **11**: 874, 1869.

9. von Rokitansky, C.: Lehrbuch der pathologischen Anatomie, Vienna, W. Braumüller, 1856, vol. 2.

blastoma, of Mallory;[10] meningoblastoma, of Oberling;[11] meningioma, of Cushing;[12] meningeal fibroblastoma, of Penfield;[13] and neuro-epithelioma, of Roussy and Cornil.[14] These titles were all employed to designate one and the same type of tumor and thereby served to create terminological confusion; yet this very list of discordant names bears testimony to the many determined efforts made to solve the intricate problem of the source and nature of the so-called dural endothelioma.

Out of these efforts grew the present day recognition that this tumor is derived from some component of the meninges, probably from embryonal rests in the arachnoid. Beyond this, however, there is no agreement. Indeed, there are few left who cling to the old concept that the tumor is of dural derivation. They are forced into the background by the larger contingent of observers who place the ultimate origin of this tumor in the embryonal arachnoid rests. More recently, encouraged by the unconfirmed views of Harvey and Burr[15] that the leptomeninges are derived from the neural crest, some investigators have made a strong plea for the neuro-ectodermal origin of most of these tumors.[11] Others have traced the origin of some to islands of glial tissue presumably displaced into the meninges in the course of the normal glial migration.[14] Then, there are those who brush aside the question of the ultimate origin of this tumor and without clearly defining their position venture the opinion that the tumor under discussion is not endothelial in character nor glial in origin but fibroblastic in structure.[16] Finally, there are some[17] who see the problem of the origin of this tumor as hopelessly confused but nevertheless undertake to classify it on the basis of unproved histogenetic factors. They have assumed that partly differentiated cells are responsible for the tumor formation and that the divergence in the character of such embryonal cells is the cause of parallel divergence in the ultimate cellular structure of the tumor in

10. Mallory, F. B.: The Type Cell of the So-Called Dural Endothelioma, J. M. Research **41**:349, 1920.

11. Oberling, C.: Les tumeurs des méninges, Bull. Assoc. franç. p. l'étude du cancer **11**:365, 1922.

12. Cushing, H.: The Meningiomas (Dural Endotheliomas): Their Source, and Favoured Seats of Origin, Brain **45**:282, 1922.

13. Penfield, W.: Encapsulated Tumors of the Nervous System, Surg., Gynec. & Obst. **45**:178, 1927.

14. Roussy, G., and Cornil, L.: Les tumeurs méningées, Ann. d'anat. path. méd.-chir. **2**:62, 1925.

15. Harvey, S. C., and Burr, H. S.: The Development of the Meninges, Arch Neurol. & Psychiat. **15**:545 (May) 1926.

16. Mallory.[10] Penfield.[13]

17. Bailey, P., and Bucy, P. C.: The Origin and Nature of Meningeal Tumors, Am. J. Cancer **15**:15, 1931.

question. Accordingly, the primitive meningeal tissue, from which the so-called meningioma is presumably derived, contains at one time or another cell forms sufficiently differentiated to assume the character of the fibroblast, the meningoblast, the osteoblast, the angioblast and the melanoblast. Each of these cell forms, when endowed with a neoplastic potency, may contribute to and often dominate the cellular make-up of the resultant tumor and so determine its character. It is in this way that meningeal neoplasms are identified as fibroblastic, melanoblastic, osteoblastic and angioblastic varieties.

Acceptance or rejection of any of the several hypotheses proffered for the establishment of the origin and identification of the character of the meningeal tumor calls for a critical survey of the data advanced in their support. Mallory's [10] observations, carried out with special staining methods, led him to express the conviction that the tumor, then termed dural endothelioma, takes its origin from arachnoid rests. These rests are little clusters of "epithelial" cells which are regularly observed in the normal arachnoid, particularly over the crests of the pacchionian bodies (figs. 4 to 6), and not infrequently as isolated cell groups scattered between layers of the dural tissue. Mallory was impressed by the staining reactions of these cells, which revealed a capacity to produce fibroglia and collagenous fibrils, and decided to group them with the fibroblastic series. Thus, in view of the presumable origin of this tumor from the embryonal rests in the arachnoid villi and the fibroblastic characteristics of its cells, he recommended the name "arachnoid fibroblastoma." Mallory apparently was not aware that Rokitansky [9] long before him had spoken of cancer of the arachnoid and that Cleland [18] as early as 1864 and Schmidt [19] more recently had suggested the arachnoid origin of this tumor, basing their views on the analogous appearance of the cell form and cell grouping observed in the tumor with that noted in the pacchionian bodies. Mallory, however, while emphasizing the arachnoid origin of the tumor, did not find it necessary to account for the origin of all its histologic constitutents, beyond making a cursory remark in which he traced collagenous fibers and blood vessels to the dura. While at times these components (collagenous fibers and blood vessels) are not abundant, their dominance at other times may overshadow the "epithelial," "endothelial" or "fibroblastic" derivatives of the "arachnoid." It is obvious that more serious thought must be given to the meningioma or "arachnoid fibroblastoma" of Mal-

18. Cleland, J.: Description of Two Tumors Adherent to the Deep Surface of the Dura Mater, Glasgow M. J. **11**:148, 1863-1864.

19. Schmidt, M. B.: Ueber die Pacchionischen Granulationen und ihr Verhältnis zu den Sarcomen und Psammomen der Dura Mater, Virchows Arch. f. path. Anat. **170**:429, 1902.

lory, in which numerous blood channels of the capillary or sinusoid variety dominate the structural character of the tumor, and to the tumor in which robust bundles of collagenous fibers directly continuous with the collagenous structure of the dura encircle cellular nodules of the type of the arachnoid rest. It is doubtful whether all these structural elements can be derived from the epithelial-like cells in the arachnoid. Some cells less restricted in their mesenchymal potencies are more likely the source of origin.

In the other part of his thesis, Mallory emphasized that the dominant cell type in the outspoken meningioma, though it has many of the morphologic features of endothelium, is fibroblastic. Granting the histologic criteria for the probable fibroblastic character of the cell in the meningioma, the fact still remains that the endothelial cells are known to be capable of forming fibroblasts under pathologic or abnormal conditions (Maximow [20]). Then, of course, the capacity of a cell to form fibroglia or collagenous fibers does not necessarily deprive it of its endothelial character nor the resultant tumor of being at least partially endothelial in origin.

In approaching the view of Oberling [11] one is confronted with a highly speculative hypothesis, which is based on an assumption rather than on fully established observations. He presupposed, but did not prove, the existence of an unripe, special cell form which he termed "meningoblast." He further assumed that this cell, in its elaboration of the riper elements of the meninges, is capable under certain conditions of giving rise to a neoplasm, for which he accordingly adopted the name "meningoblastoma." Oberling, bearing in mind the work of Harvey and Burr,[15] assumed further that many, if not all, of the so-called meningoblasts are actually neuro-ectodermal elements which, not unlike the Schwann cells of the peripheral nerves, have come from the neural crests. Thus, he found a ready explanation for tumor of the meninges in which the cellular elements assume the character of diffuse gliosis. He was in part supported by Roussy and Cornil,[14] who accepted the probable existence of the meningoblast, though they were inclined to consider it as mesodermal in origin. They, too, favored the view of the existence of a glial meningeal tumor but traced it to unripe glial elements which had strayed into the meninges during the period of normal glial migration. Lodged there in the form of heterotopias with neoplastic potencies, they were believed to produce tumor formations. Unfortunately for the last two attractive hypotheses, there are no reliable observations as to the existence of the so-called meningoblast. The meninges are noted for their failure to exhibit at any period of

20. Maximow, A. A.: A Textbook of Histology, Philadelphia, W. B. Saunders Company, 1930.

development cell forms with definite morphologic orientation except those which seem to assume the character of unripe endothelium. No less significant is the fact that glial heterotopias in the meninges are exceedingly rare and are demonstrable only in the rare types of developmental disturbance, such as tuberous sclerosis, or in the still rarer instances of congenital chronic inflammatory disease of the brain and meninges. In the last condition migration of glia cells may take place into the meninges. In the case of Globus,[21] cited by Bailey and Bucy,[17] only a few mature glia cells were seen invading the leptomeninges along the course of an occluded blood vessel, at points where the meninges were fused with the underlying cortex.

Penfield,[13] who expressed full agreement with the observations of Mallory, was disinclined to accept any of the views of the French school and suggested the inclusion of the tumor among the encapsulated fibroblastomas. As has already been said, while the fibroblastic character is not denied for many of the cellular elements in a large number of meningeal tumors nor for the dominant cell type of a few, the acceptance of this view does not in any way deny the endothelial character of the majority of the tumors nor the meningeal origin of all. Hence, the term "fibroblastoma" is not descriptive of the majority of meningiomas, nor is it justified by their probable source; it can be applied only to a small subgroup in which dural derivatives form the exclusive or predominant contents.

PHYLOGENETIC THEORY OF ORIGIN OF THE MENINGIOMA

It appears, then, that none of the views advanced for the origin and structural forms of the tumor are in keeping with the known facts. Hence, it would seem appropriate to examine a new thesis concerning the origin and diversity of structure of the so-called meningioma based on the concept of the phylogenesis and ontogenesis of the meninges.

In the early stage of development of the head and its enclosures, the medullary tube is enveloped by a layer of mesenchyme which spreads uninterruptedly between the underlying primitive nervous system and the skin. A little later the anlagen of the skeletal structures of the skull and spine appear; the greater part of the mesenchyme, however, still remains as a uniform layer of undifferentiated tissue completely filling the space between the primitive brain tissue and the developing cartilaginous or bony tissue of the skull (fig. 1). At this time it embodies the primordium of all the meningeal coverings as well as that of the

21. Globus, J. H.: A Contribution to the Histopathology of Porencephalus, Arch. Neurol. & Psychiat. **6**:652 (Dec.) 1921.

periosteum. Hallerstein [22] spoke of this layer as the skeletoneural intertissue. In an early stage of its differentiation the skeletoneural intertissue splits off the periosteum of the skull. This is followed by the separation of the dura, or pachymeninx, from the leptomeninx, the

Fig. 1.—The primitive meninx (or skeletoneural intertissue) in a 12 mm. pig embryo (× 340). *M* indicates mesenchyme; *P*, early pial formation, and *Med*, the medullary tube.

latter subsequently splitting into the arachnoid and the pia (figs. 2 and 3). As to how this process of differentiation proceeds there is diversity

22. von Hallerstein, V. H.: Hüllen des Zentralnervensystems, in Bolk, L.; Göppert, E.; Kallius, E., and Lubosch, W.: Handbuch der vergleichenden Anatomie der Wirbeltiers, Vienna, Urban & Schwarzenberg, 1934, p. 309.

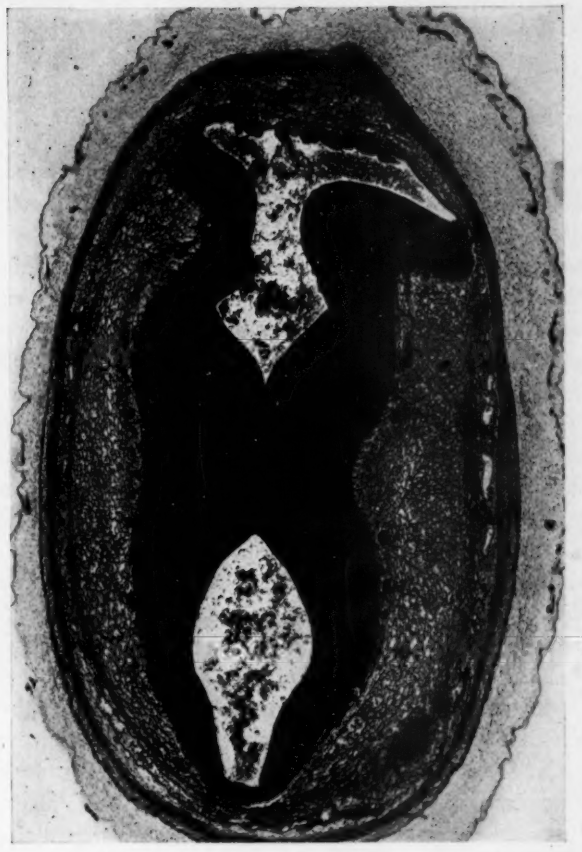


Fig. 2.—The primitive meninges with zones of cellular condensation (ectomeninx and endomeninx) in a dog embryo (× 20).

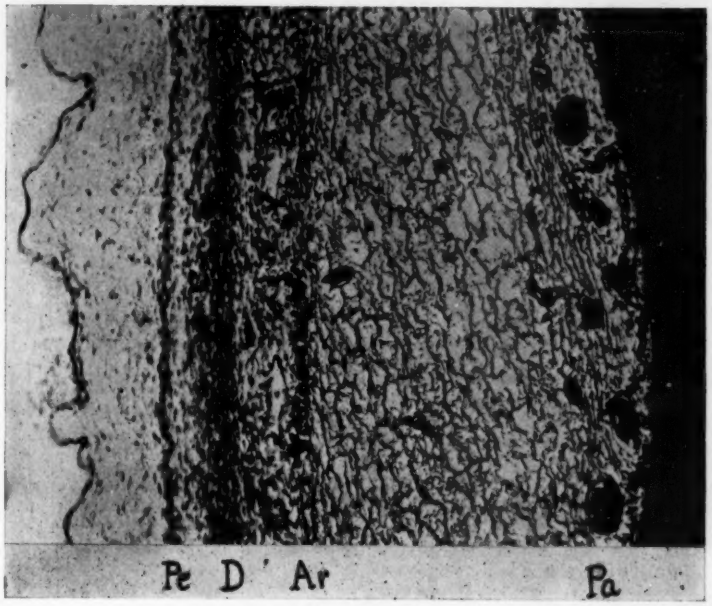


Fig. 3.—The primitive meninges with the zone of condensation indicating the primordia of (*Pe*) the periosteum, (*D*) the dura, (*Ar*) the arachnoid and (*Pa*) the pia (× 120).

of opinion. According to Sterzi,[23] the following events mark the course of the full development of the meninges: The skeletoneural intertissue first gives rise to two readily distinguishable parts—an internal and an external. The internal part, which is in direct contiguity with the brain, is the so-called meninx primitiva and is distinctly recognizable in cyclostomes and fishes. The external part of the skeletoneural intertissue is at first subjacent to the ectoderm, or skin. In its differentiation it gives rise to the so-called periosteum of the cranium. While it obviously does not play a rôle in the formation of the meninges, its close, though transient, association with the meninx primitiva is important and should be recalled when the occurrence of bone in the meningeal tumor is discussed. The meninx primitiva and the periosteum are at first held together by a zone of loose tissue, which Sterzi designated as the perimeningeal layer. In amphibians and reptiles the primitive meninx splits off a dense layer, which forms the dura, or pachymeninx. With this separation of the dura, the residual part of the meninx primitiva becomes the meninx secondaria. In birds, on the one hand, the secondary meninx shows the first signs of undergoing further cleavage into the arachnoid and the pia, a process which is most pronounced in mammals. On the other hand, a reversal in the general process of cleavage in the primary meninx takes place in reptiles and birds, in which the dura fuses with the cranium while the perimeningeal tissue, which at one time fused the primary meninx with the periosteum, disappears.

Geldern [24] gave a somewhat different version of the development of the meninges. He regarded the entire mesenchyme lodged between the ectoderm and the medullary tube as the primitive meninx. Somewhat later in embryologic development, the part which is directly contiguous to the nervous system is distinguished as the endomeninx, and the outer part which is close to the skeleton, as the ectomeninx. Between these two zones there is a layer of loose tissue, which Geldern called the intermeningeal tissue. This arrangement is observed in the cyclostomes and fishes. Higher in the vertebrates, in amphibians and reptiles, the ectomeninx splits further into the periosteum and the dura. In birds and mammals the periosteum and the dura fuse again and form the so-called secondary dura. The endomeninx remains as a single layer until birds and mammals are reached. There it splits into the arachnoid and the pia. The intimal portion of the pia is closely adherent to the brain wherever it follows the entering blood vessels. It is an exceedingly thin membrane, consisting only of a layer of poorly defined cells and becoming still thinner as it enters the brain. This thin covering

23. Sterzi, G.: Recherches sur l'anatomie comparée et sur l'ontogénèse des méninges, Arch. ital. de biol. **37**:257, 1902.

24. van Geldern, C.: Ueber die Entwicklung der Hirnhäute bei Teleostieren, Anat. Anz. **60**:48, 1925-1926.

was named by Held the membrana accessoria. As it extends with the blood vessels into the brain substance, this membrane bounds externally the so-called perivascular space of Virchow and Robin.

It is obvious from the foregoing account that at one stage in the phylogenetic and ontogenetic development of the meninges, the bone-forming periosteum, the collagen-producing anlage of the dura, the anlage of the epithelial (endothelial or mesothelial) covering of the arachnoid and the primordium of the vascular covering, the pia, are fused into a single mesenchymatous layer, the skeletoneural intertissue of Hallerstein, or the meninx primitiva of Geldern. At no time in the development of the meninges can there be distinguished unripe elements of the type spoken of as meningoblasts or primitive cells of the glial variety, such as spongioblasts. All that can be said with certainty is that unripe primitive elements must exist in the meningeal anlage and may continue to exist for some time during the process of meningeal formation. At this point it may be recalled that embryonal remnants resembling the structure of the arachnoid are frequently seen in the normal meninges (figs. 4 and 5) and that islands of poorly differentiated meningeal tissue (fig. 4*A*) are often observed in malformed brains, particularly in conditions causing communicating hydrocephalus. To this may be added a less widely known fact that alongside these embryonal residuals there are often psammoma bodies (fig. 5*B*), structures which are pathognomonic of meningeal tumor, particularly of the psammomatous variety. Of significance also are the melanophores, or melanin-carrying cells, seen in variable numbers in the normal meninges (fig. 6). The occurrence of the structures enumerated in the normal meninges, particularly when they constitute embryonal rests, readily explains how a meningioma may acquire the character of any of the several forms of meningeal tumor to be described.

It seems reasonable to assume, since the tumor in question is derived from the primitive meningeal material which incorporates in itself the primordia of the several layers of the mature meninges as well as that of the periosteum, that it is likely to acquire the character of any one of the component layers of the meninges and to embody in varying degrees the features of any or all of the component parts of these coverings, including occasionally bony structures traceable to the periosteal anlage in the skeletoneural intertissue. Moreover, since the early stage of formation of the meninges coincides with the migration of the cells of the neural crests as they proceed to form the dorsal roots and sympathetic ganglia, it is not unlikely that neuroblasts and spongioblasts may stray from the stream of migrating cells and become enmeshed among the mesodermal elements of the meninges. This may explain the occasional occurrence of tumors which bear a strong resemblance to neuroblastoma and, less frequently, to spongioblastoma.

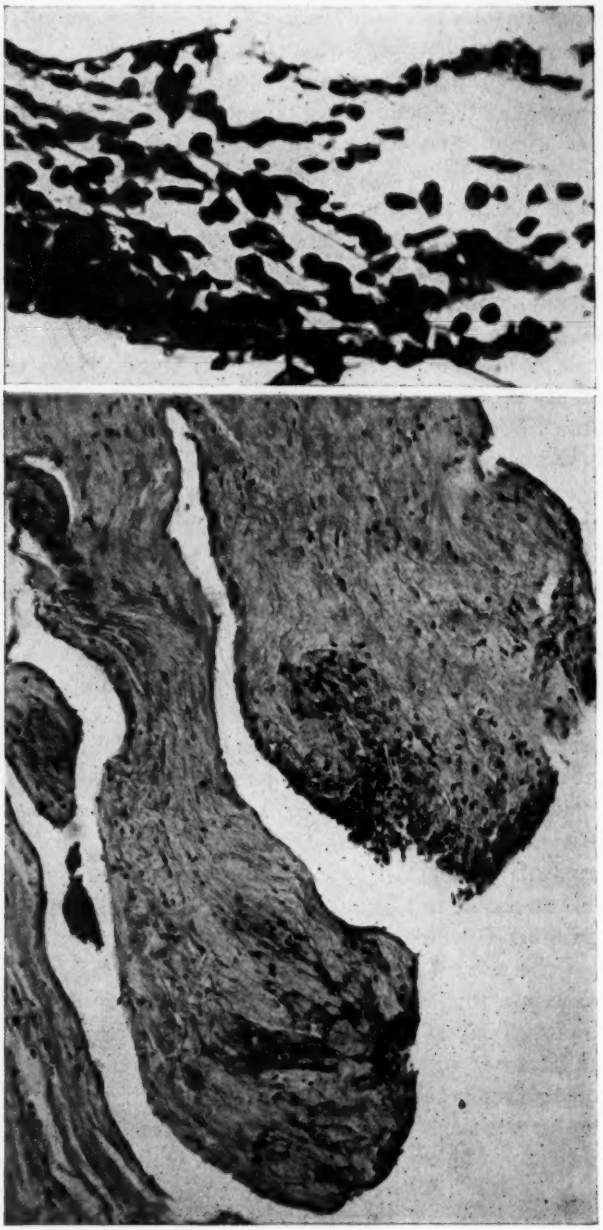


Fig. 4.—(*A*) Section of the meninges in a case of communicating hydrocephalus, at a point where the leptomeninges failed to split into the pia and the arachnoid (× 240) and (*B*) crest of a normal arachnoid villus covered and infiltrated with arachnoid (epithelial?) cells (× 120).

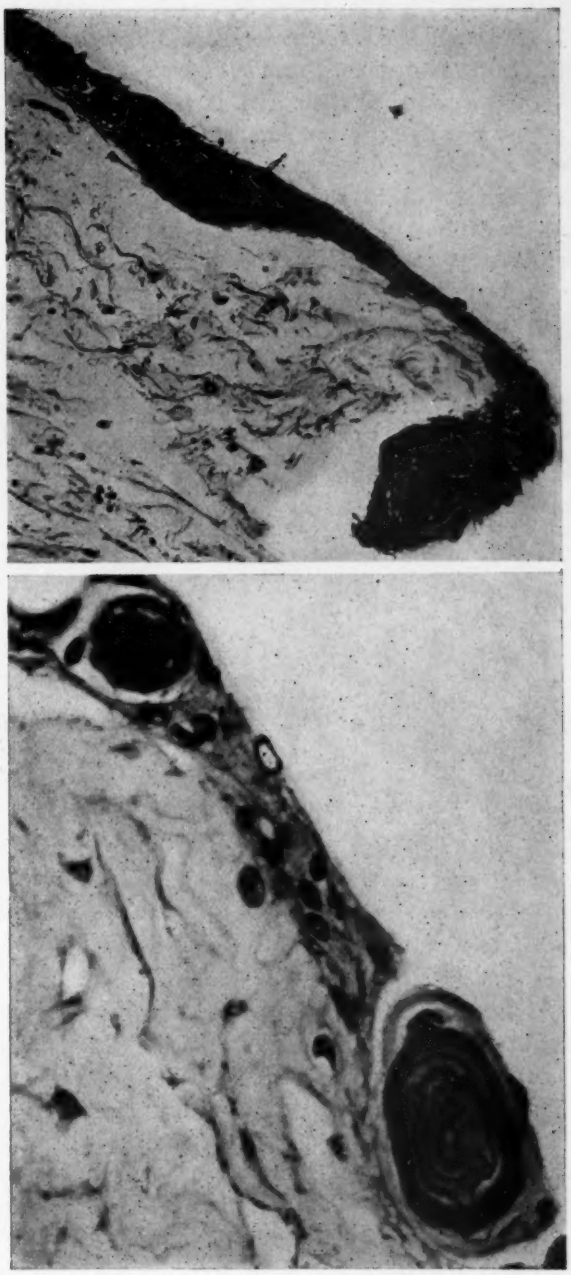


Fig. 5.—(*A*) Arachnoid remnants in the normal meninges (× 200) and (*B*) psammoma bodies in the normal pia (× 640).

TYPES OF TUMORS DERIVED FROM PRIMITIVE MENINGEAL TISSUE

TYPE I.—*Meningioma Indifferentiale; Mesenchymatous Meningioma.*—This form of meningeal tumor duplicates the mesenchymatous structure of the meninges in their earliest period of development. In it, the cell form and the cell arrangement which are characteristic of mesenchyme are retained to a great extent, alongside areas in which the cells assume a vascular or an angioblastic character.

The gross appearance of such a neoplasm has no distinctive character and does not differ from that of the average meningioma. It, too, gives

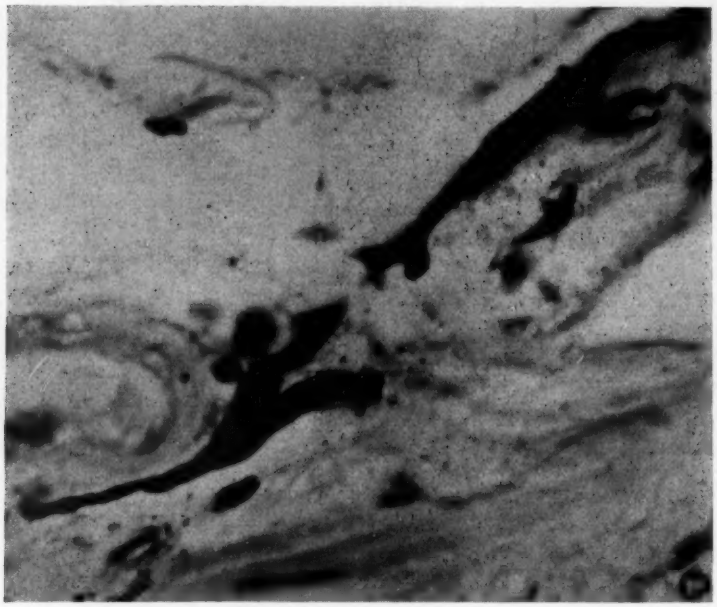


Fig. 6.—Chromatophore in the normal pia (× 240).

the false impression of being encapsulated and sharply demarcated from the adjoining brain tissue. Of some significance here is the presence of a large number of prominent vessels traversing the surface of the tumor. A tumor of this type is readily enucleated and thus emphasizes the impression of being completely separated from the surrounding brain tissue. This, however, as will be seen from subsequent descriptions, proves not to be the case when the tumor is studied histologically.

The cellular make-up of this type of tumor in its major part (fig. 7*A*) bears a strong resemblance to the mesenchymal structure of the meningeal primordium, while in other parts the cellular elements resemble closely the primitive vascular endothelium (fig. 7*B*). With low magnification the distinction between the two dominant cell types

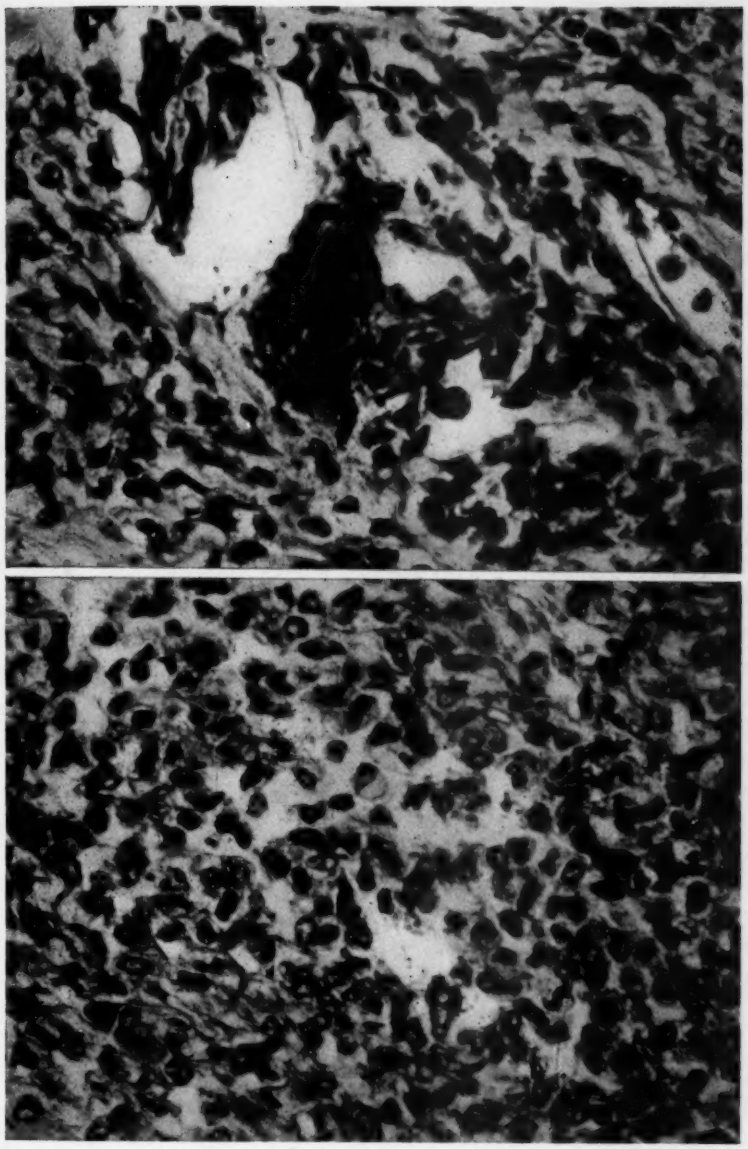


Fig. 7.—(*A*) Mesenchymatous form of meningioma (× 520). Cell structure, to be compared with that shown in figure 4 *A*, and (*B*) vascular endothelium in parts of the tumor.

is almost unrecognizable, but the general structure of the tumor assumes a more characteristic organization. There come into view many blood channels scattered regularly throughout the field—some filled with blood and others free. They alternate with cellular collections which give the impression of germinal centers (fig. 8*A*). These groups are not unlike blood islands, although, aside from several poorly formed polymorphonuclear leukocytes, the cells have not acquired the structure of mature or immature blood elements. With higher magnification many such areas often show central zones of "liquefaction" occupied by variable amounts of a serous fluid in which are seen "floating" a few blood elements and primitive vascular endothelium (fig. 8*B*). Newly formed capillaries often can be seen at the periphery of such areas. In other parts of the tumor these areas of "liquefaction" are characterized by numerous cells not unlike compound granular cells. These cells bear a close resemblance to the "foam cells" observed in the Lindau type of hemangioblastoma of the cerebellum. Since special stains do not disclose any fat deposits within these cells, they are probably not compound granular cells mobilized in an area of necrobiosis but evidently the "foam cells" typical of the aforementioned vascular tumor (fig. 9*A* and *B*). No less significant is the fact that the neoplastic tissue can be seen to be in direct continuity with the pial membrane (fig. 10*A*), the latter becoming the so-called capsule, which is present only on the exposed part of the tumor. What is usually known as a capsule is in reality little more than a prolongation of the pia, which, in fact, is to a great extent the source of the tumor. Finally, thorough search will disclose areas in which tumor cells are often arranged about blood vessels in a peritheliomatous fashion, not unlike that seen in primary sarcoma of the brain (fig. 10*B*).

It is obvious, then, that in meningioma indifferentiale, alongside the mesenchymal structure characteristic of the meningeal primordium, there are readily recognized areas with morphologic orientation in the direction of vascular tissue, duplicating to some extent the pial layer of the leptomeninges. However, this vascular orientation is not limited to the mesenchymatous form of meningioma but can be detected in practically every form of tumor derived from the meninges. It would seem to indicate that a vascular component in the skeletoneural intertissue, which may be regarded as the primordial structure of the pia, has a greater growth tendency and therefore is dominant in the majority of meningeal tumors. In many tumors of this derivation the vascular components at times grow faster and more profusely than the other primordial elements and completely overshadow the other tissues. Thus Golgi's [8] concept of the endotheliomatous character of this tumor was not without foundation and the long-lived term "dural endothelioma" was not without good reason.

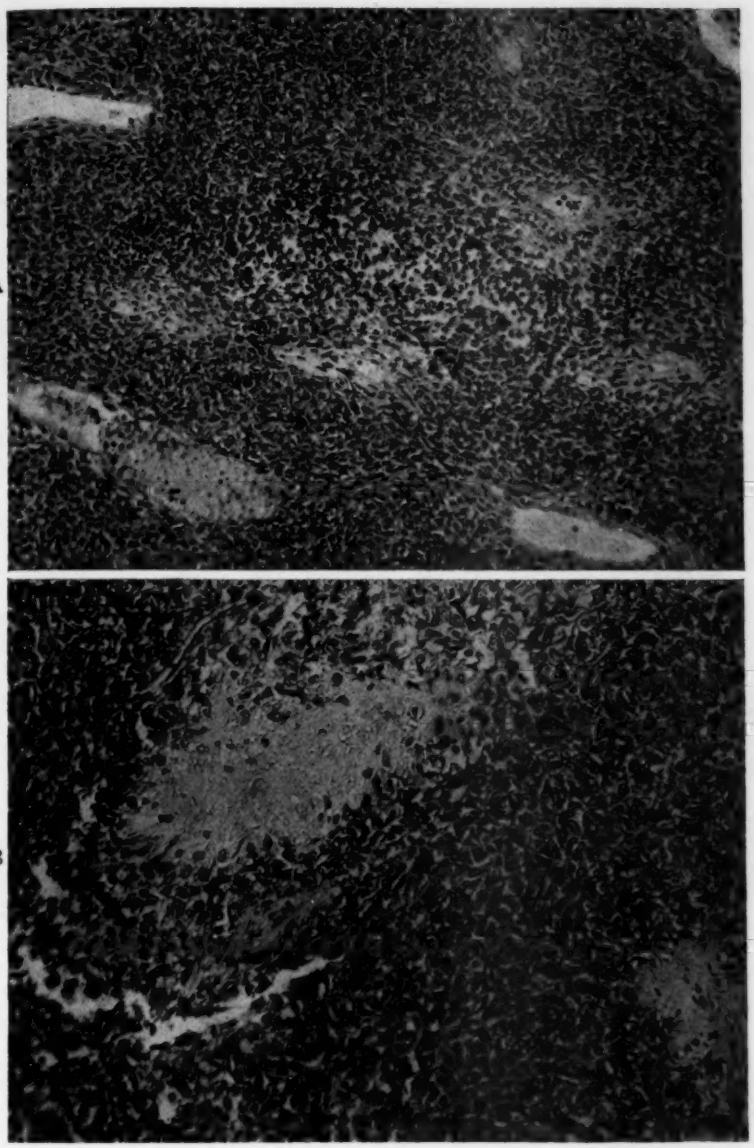


Fig. 8.—(*A*) Mesenchymatous form of meningioma. Vascular channels and germinal centers (× 160) and (*B*) areas of liquefaction (× 340).

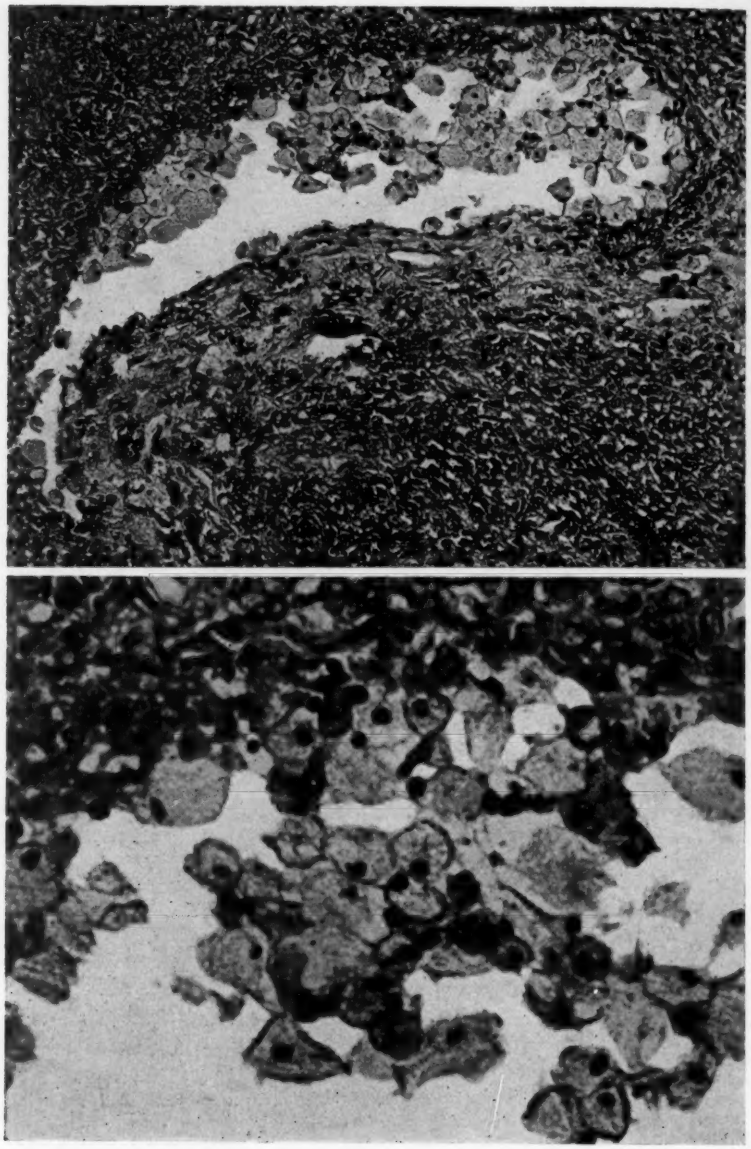


Fig. 9.—(*A*) Foam cells in areas of "liquefaction" (× 160) and (*B*) transition of the solid endothelial cells into "foam cells" (× 420).

TYPE II.—*Meningioma Omniforme; Primitive Meningioma.*—This type of meningeal tumor assumes a structure in which all four elements of the skeletoneural intertissue are represented in a somewhat more

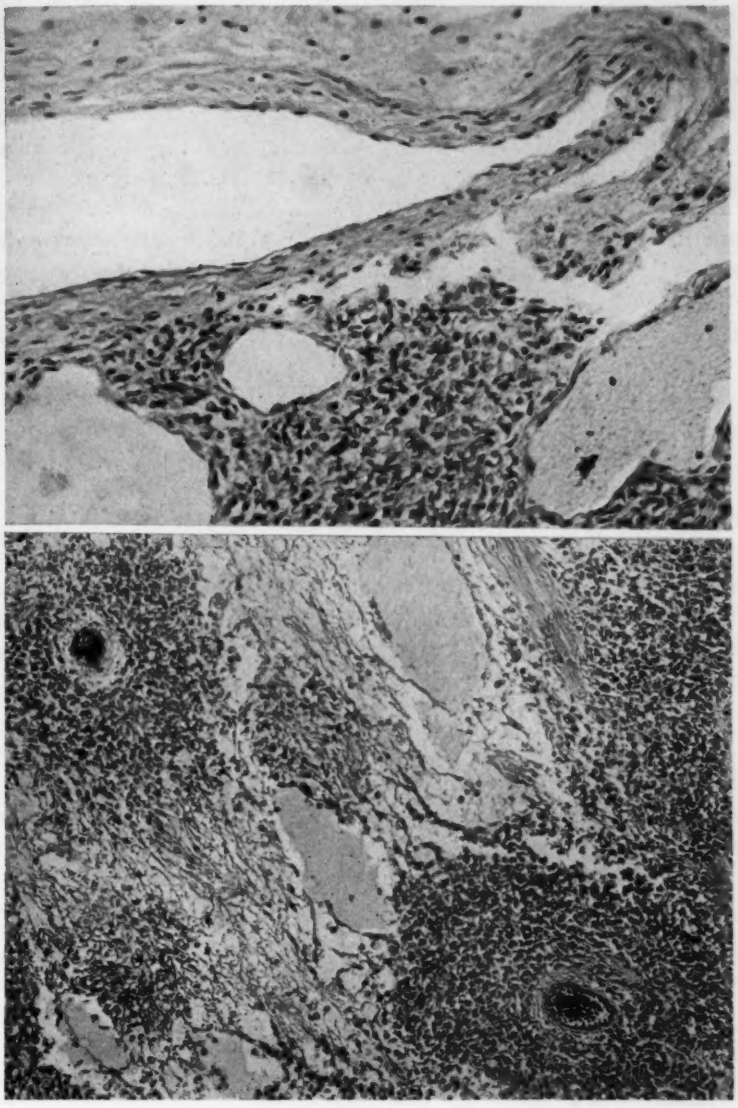


Fig. 10.—(*A*) Fusion of the tumor with the pia (× 200) and (*B*) sarcomatous islands in the mesenchymatous form of meningioma (× 120).

differentiated form, in accord with the stage in the development of the meningeal coverings which is coincident with the cellular condensation and splitting of the primary meningeal layers (fig. 3).

This tumor does not differ in gross appearance from the previous type, and though in the light of its probable origin it should be more peripheral than cortical in location, it nevertheless may assume a central position (fig. 11 *A*) in which the tumor can be seen to be intimately related to the surrounding brain tissue.

The histologic structure of the tumor in its major portion may assume a more or less uniform character, not unlike that seen in the previous type (fig. 11*B*). However, careful study of sections obtained from various parts of the tumor will disclose that it had acquired a higher differentiation in some of its parts. Thus, alongside the more or less free and undifferentiated cell forms (fig. 12*A*) there are noted numerous well developed capillaries, strikingly similar to those encountered in the young pia (fig. 12 *B*). Bone in various amounts and various stages of differentiation is also observed (fig. 13*A*), indicating the early and intimate relationship existing between the endosteal component from which it arises and the primitive meninges. There is also a rather substantial quota of collagenous fibers (fig. 13*B*) originating from the dural component of the pachymeninx. Large accumulations of cells resembling epithelium or endothelium, either in flat syncytial sheaths or in irregular cords or whorls, all of which simulate the arachnoid remnants in the mature arachnoid, are observed side by side with other tissue structures, such as numerous sinusoids (fig. 14*A*) and equally numerous small but well formed blood vessels (fig. 14*B*). Scattered throughout the tumor are groups of cells which are in the process of vacuolation and approach the character of "foam cells." In addition to the preceding cell structures, there are often seen in segregated areas collections of pigment-carrying cells (fig. 15*A* and *B*).

Type III.—*Pachymeningioma; Fibroblastic Meningioma or Dural Fibroblastoma.*—This variety of meningeal tumor, aside from its more definite attachment to the dura (fig. 17*A*) and its harder consistence, presents no distinguishing gross features.

Microscopically, however, it is readily distinguishable from the two preceding types and from other forms to be described later. As its name suggests, it duplicates the structure of the pachymeninges by consisting predominantly of collagenous fibers and often reveals areas of calcification and bone formation. The last condition is readily understood when it is recalled that the pachymeninx is responsible for the differentiation of both the periosteum and the dura. Indeed, this type of tumor may also contain a few nests of arachnoid cells (fig. 16) and occasionally includes many degenerating capillaries or psammoma bodies (fig. 17 *B*). This is the only type of meningioma to which the term "meningeal fibroblastoma" or "dural fibroblastoma" can be applied, though the term "pachymeningioma" is preferable. It is a rather

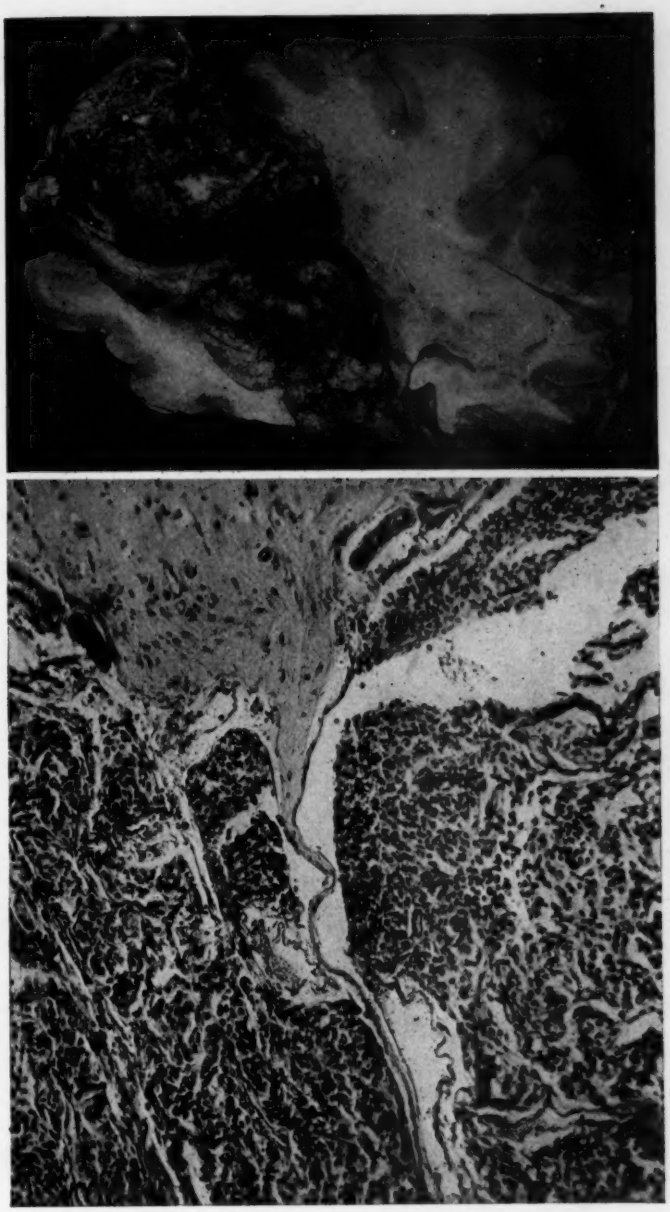


Fig. 11.—(*A*) Gross appearance of the meningioma omniforme and (*B*) histologic structure of the same type of tumor (× 150). Note the extension of pia into the neoplasm.

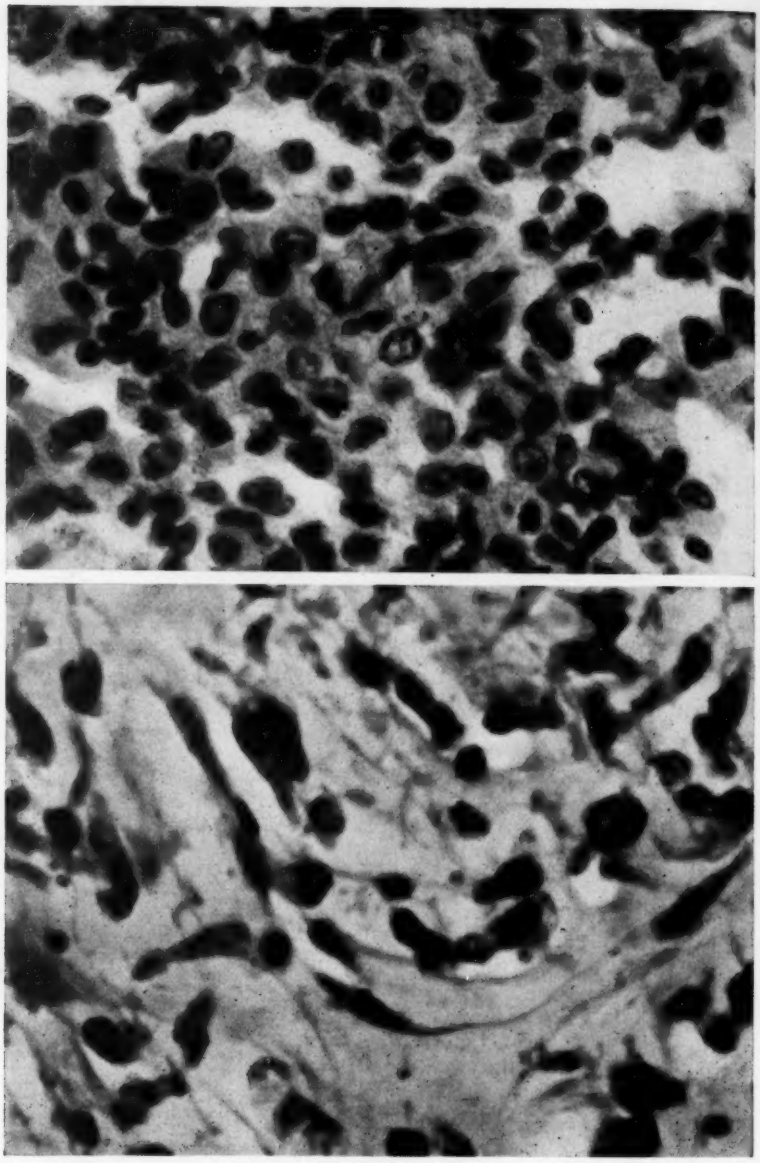


Fig. 12.—(*A*) Meningioma omniforme. Dominant type of cells (× 640) and (*B*) newly formed capillaries (× 900).

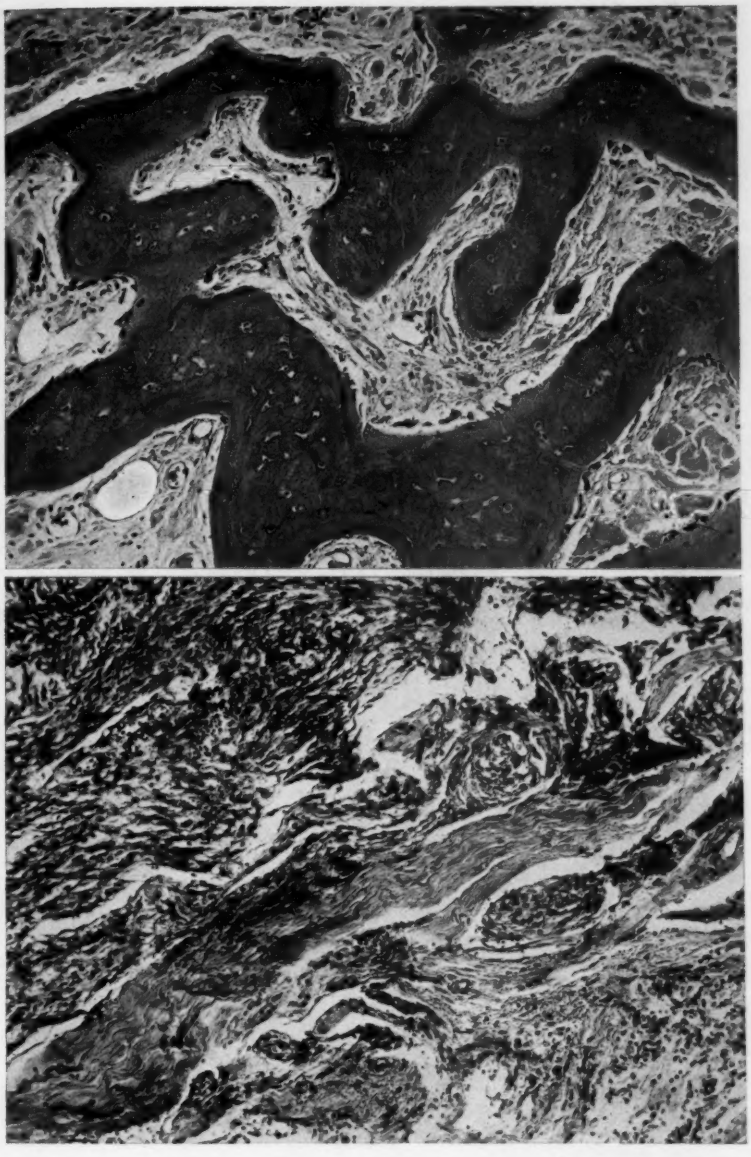


Fig. 13.—(*A*) Bone formation and (*B*) collagenous (dural) tissue in meningioma omniforme (× 150).

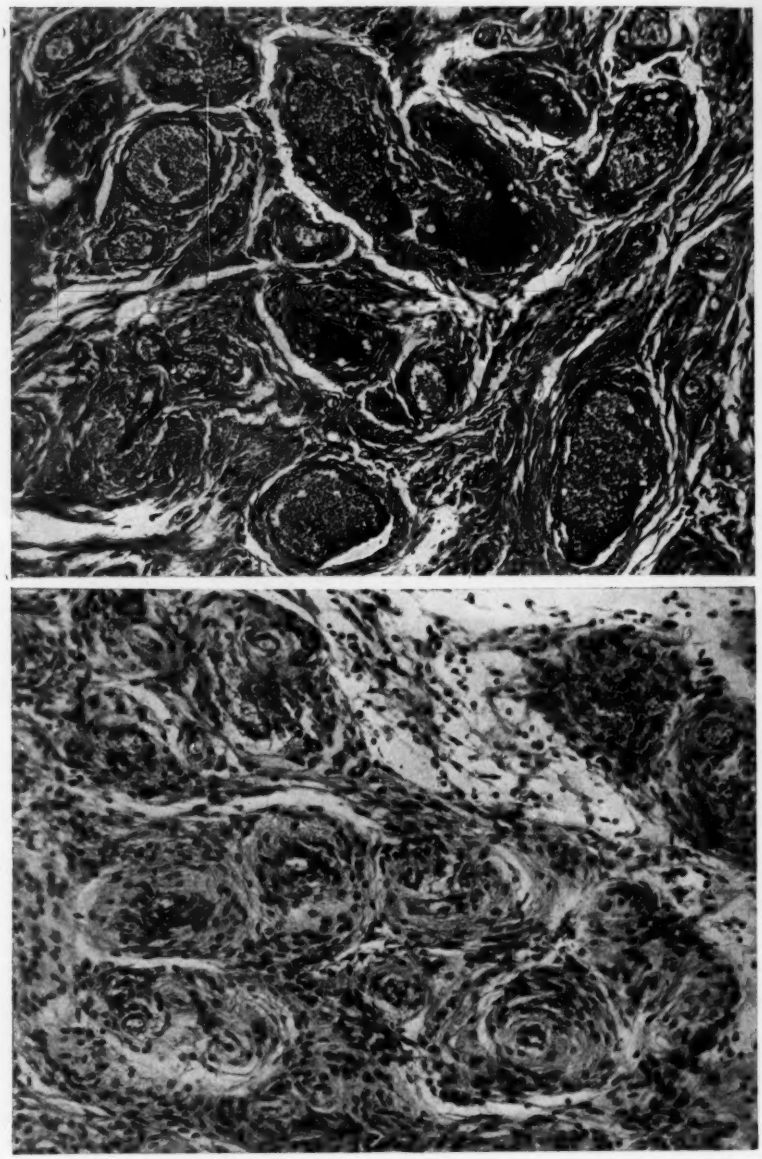


Fig. 14.—(*A*) Sinusoids in the tumor and adjacent brain tissue (meningioma omniforme) (× 150). Note the lack of separation of the tumor tissue from the overlying brain tissue. (*B*) Whorls enclosing blood vessels in a meningioma omniforme (× 170).

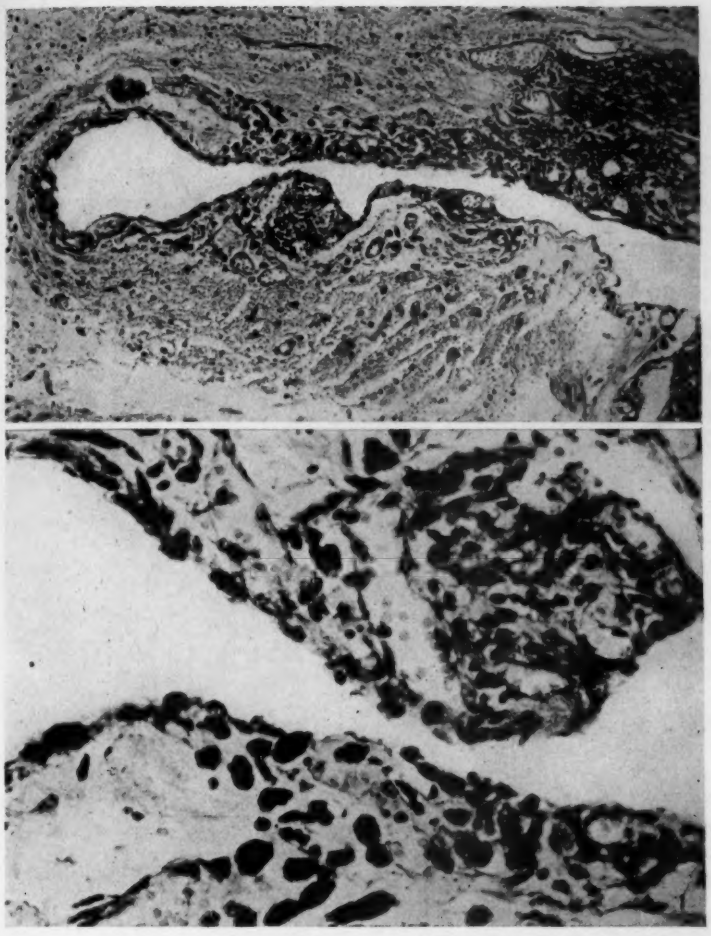


Fig. 15.—Melanoblastic areas in a meningioma omniforme; *A* (× 150) and *B* (× 400).

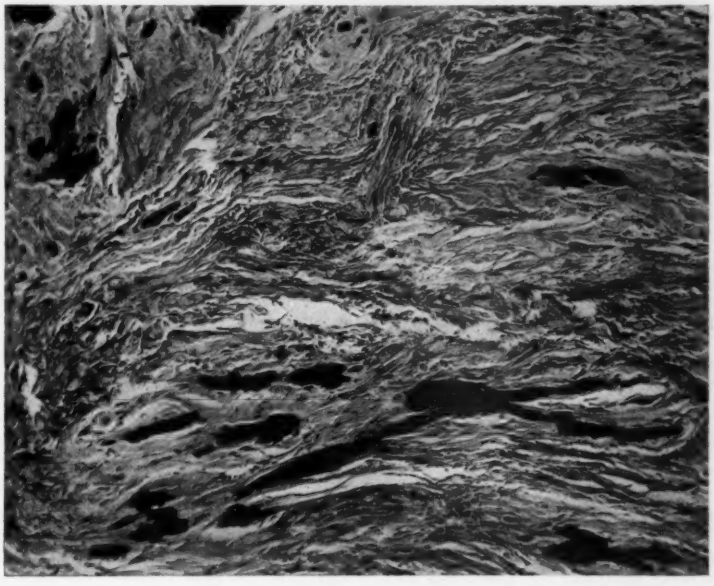


Fig. 16.—Histologic structure of pachymeningioma (dural fibroma) (× 120).

uncommon form of neoplasm and usually is detected accidentally, probably owing to the fact that it never acquires a large size and thus does not give rise to signs and symptoms detectable during the life of the patient.

TYPE IV.—*Leptomeningioma; Arachnoid (?) Meningioma.*—The fourth variety of tumor differs from the preceding forms in that it

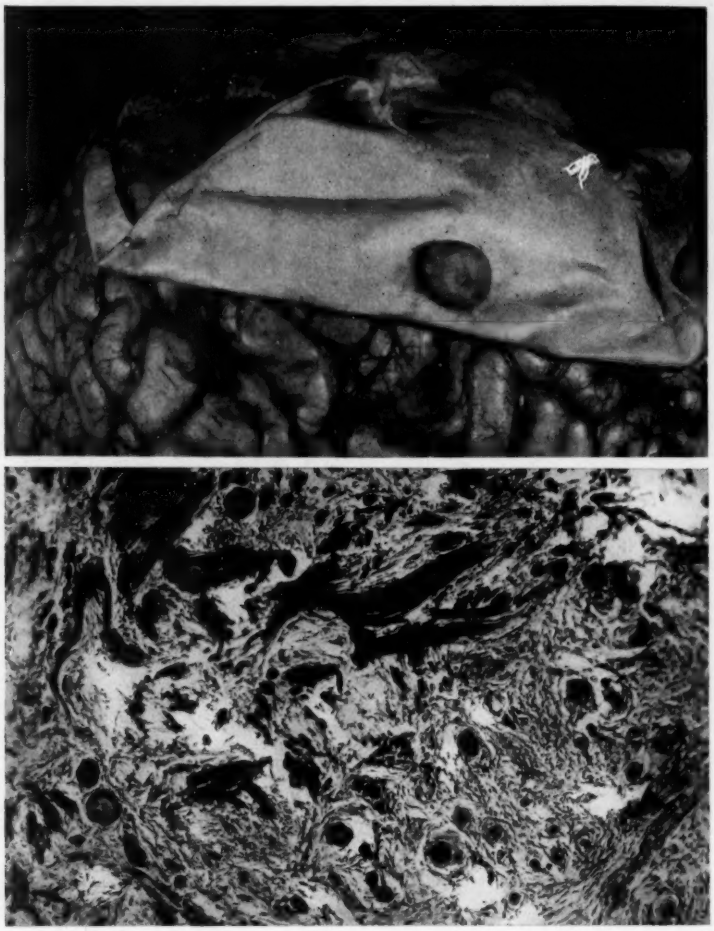


Fig. 17.—Pachymeningioma (dural fibroma). (*A*) Gross appearance and (*B*) psammoma bodies in the microscopic preparation (× 120).

reproduces in its make-up mainly structures of the leptomeninges and at times predominantly those of the arachnoid. Grossly this type of tumor cannot be distinguished from those described under types I and II. It, too, is likely to be lodged in a depression on the surface of the brain.

Histologically, however, the tumor is quite different and consists of cords of flat cells, alternating with whorl-like cell groups (fig. 18), many of which disclose in their center small blood channels. These vascular channels would seem to indicate that a sharp line cannot be drawn between the tumor components of arachnoid and those of pial derivation. Moreover, it is safe to say that there is no tumor in which the arachnoid only is reproduced, without an admixture of vascular structures, and, for that reason, it is doubtful whether there is a tumor that can be considered as a true arachnoid meningioma. Therefore, the term "leptomeningioma" is preferable for this form of neoplasm. It

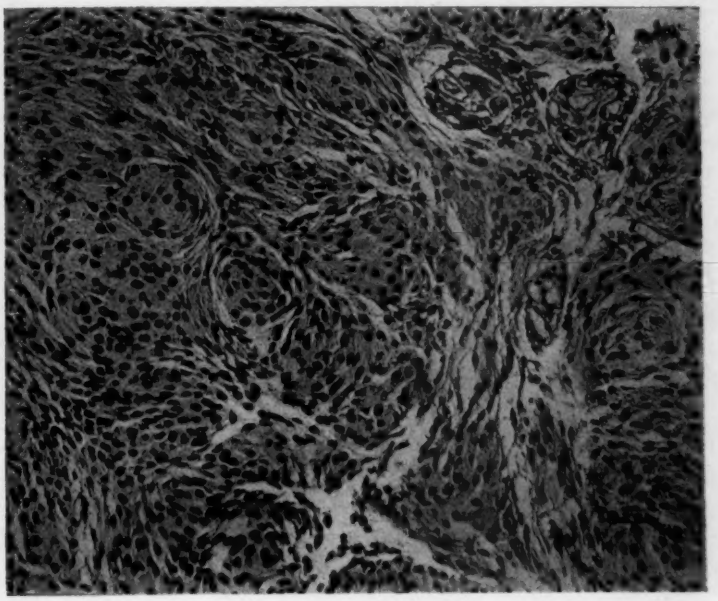


Fig. 18.—Histologic structure of leptomeningioma, predominantly arachnoid in type (× 150).

is also significant that, in spite of the fact that a line of cleavage between the tumor and the adjacent brain tissue is noted on gross inspection (fig. 19), giving the impression of encapsulation, this type of tumor is almost always invasive (fig. 20). It not only infiltrates the dura but may contain dural components within its structure. On the other hand, it can be seen to infiltrate the adjacent brain or contain brain tissue in its periphery (fig. 20 *B*).

Not infrequently, a subtype of this tumor, although grossly not readily differentiated from the preceding type, can on careful study be recognized as showing pronounced orientation toward the vascular or pial form of meningioma. Although it still gives the appearance

of being segregated from the surrounding tissue, it can nevertheless, be identified grossly by the numerous small cystlike structures seen on section (fig. 21). Its greater tendency to invaginate into the brain tissue may also be regarded as a diagnostic anatomic feature. Of still greater significance is the presence of large numbers of "foam cells," more or less irregularly but widely distributed and sometimes occurring in large collections (fig. 22 *A*). Their occurrence was already noted to a lesser degree in the preceding types of meningioma. When numerous capillaries in various stages of formation and degeneration are observed alongside the "foam cells" (figs. 22 *B* and 23 *A*), the vascular orientation of this type of tumor becomes obvious. What is still more

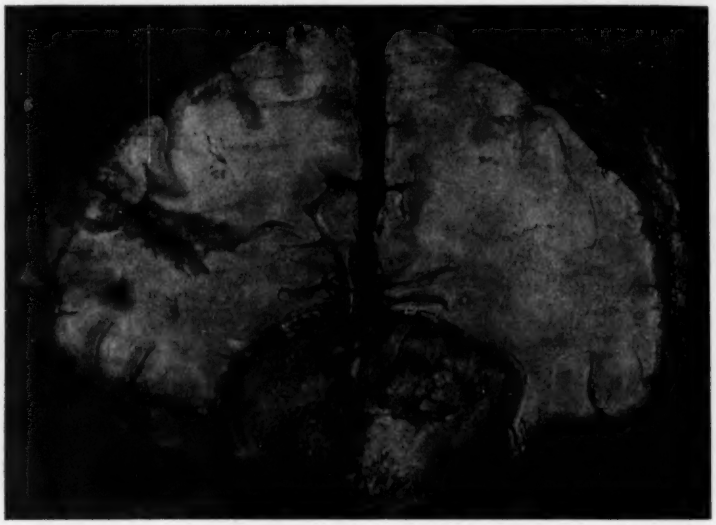


Fig. 19.—Gross appearance of a leptomeningioma, the histologic structure of which is illustrated in figures 20 *A* and *B*.

important is the frequent occurrence of islands containing numerous, exceedingly large, predominantly mononuclear, and occasionally multinuclear giant cells. They show large amounts of cytoplasm and give the impression of rapidly growing elements (fig. 23 *B*). They are not unlike the cells observed in the more malignant forms of meningeal neoplasm, such as sarcomatosis of the meninges or intracereberal sarcoma. The presence of these cells should be borne in mind when the relationship of meningioma to primary sarcoma of the meninges is considered.

Type V.—*Meningioma Piale; Pial (Vascular) Meningioma.*—The fifth type of tumor displays almost exclusively pial components, namely, capillaries, sinusoids and vacuolating (foam) cells. In this form of

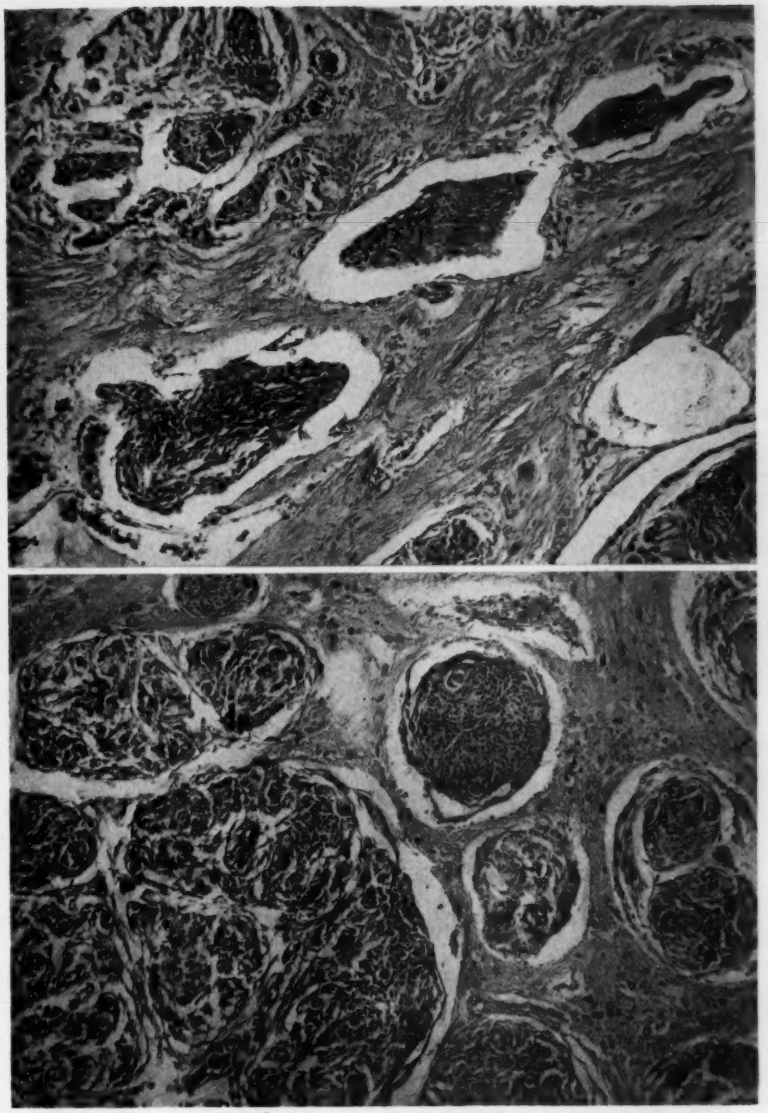


Fig. 20.—Histologic appearance of a leptomeningioma infiltrating (*A*) the dura and (*B*) the brain (× 120).

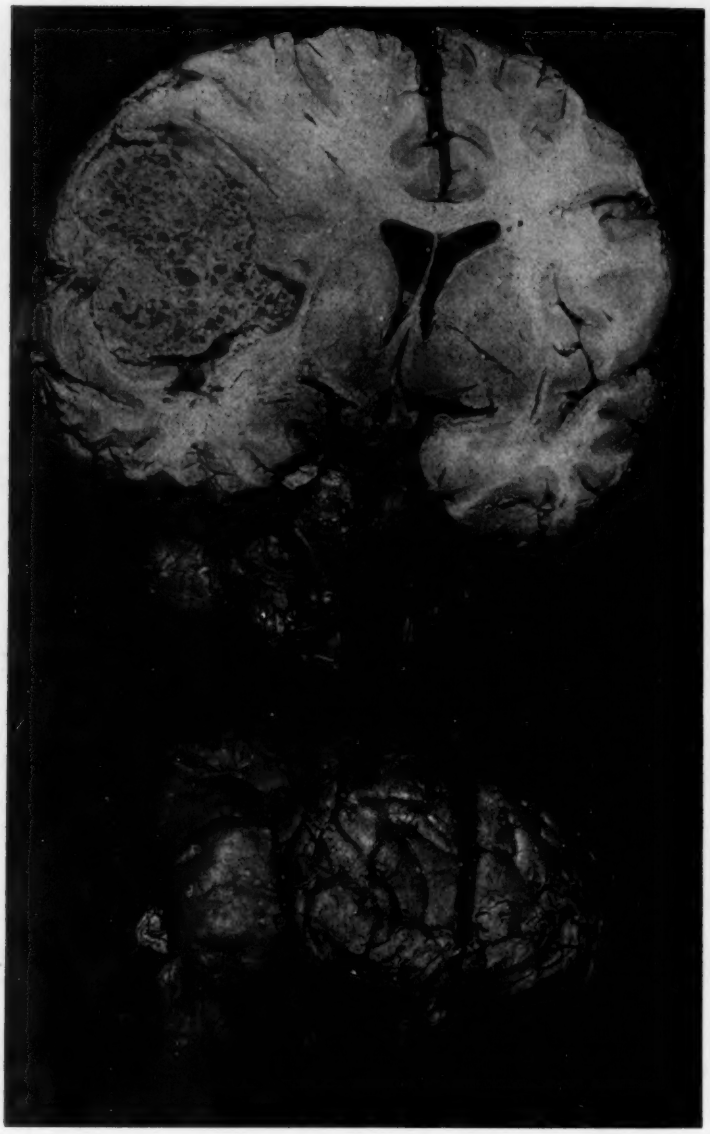


Fig. 21.—Gross appearance of a leptomeningioma with a decided vascular, pial orientation.

tumor, which is in reality an offshoot of the leptomeningioma, there are several transitional forms, in accordance with the stage of differentiation of the vascular tissue.

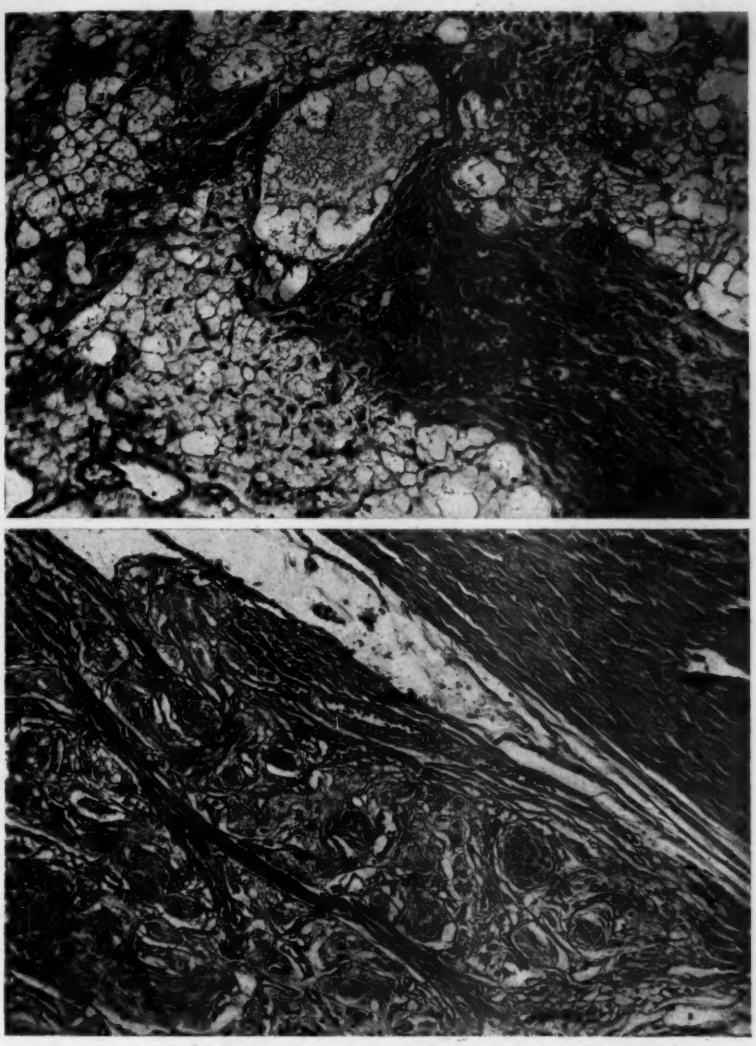


Fig. 22.—(*A*) Histologic appearance of the leptomeningioma shown in figure 21 (× 120). Note the large number of "foam cells." (*B*) Leptomeningioma with interlacing collagenous structures infiltrated by arachnoid structure (× 150).

In one subtype, the hemangio-endotheliomatous form, the gross lesion, with its deep red color, already presents the appearance of a predominantly vascular tumor (fig. 24 *A*). Histologic study of the

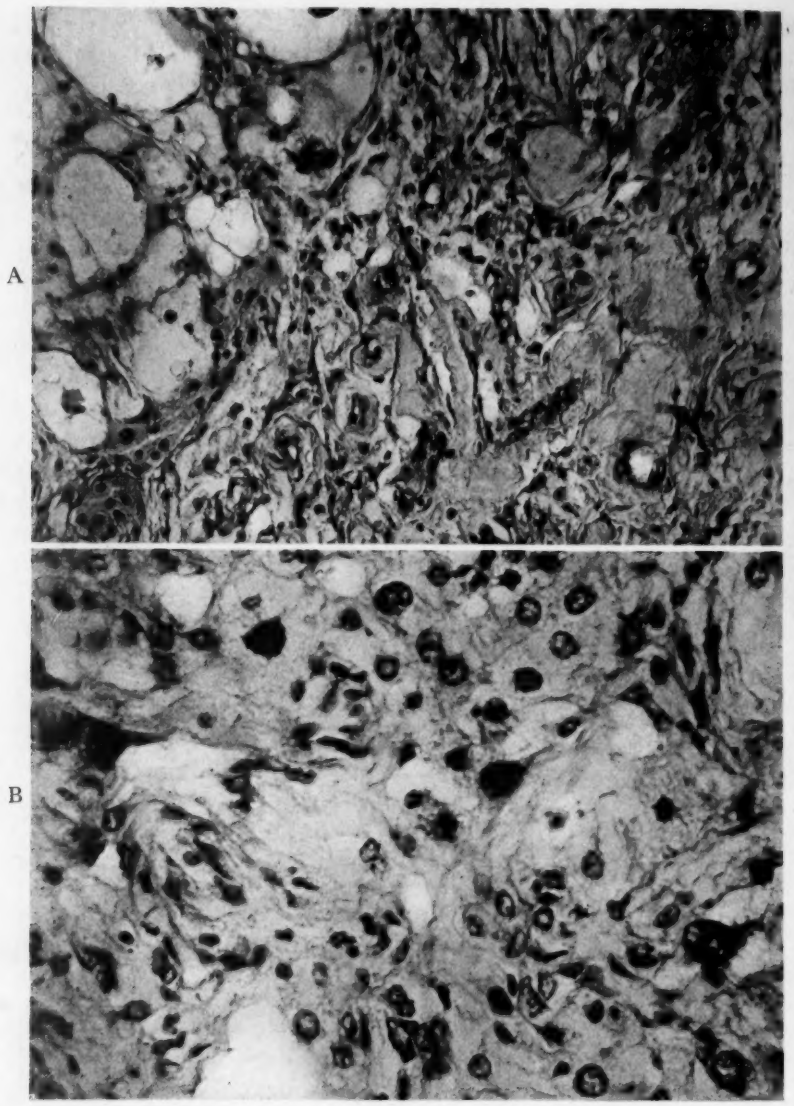


Fig. 23.—Leptomeningioma shown in figure 21, revealing (*A*) vascular (pial) components (× 200) and (*B*) tendency toward sarcomatous transition (× 520).

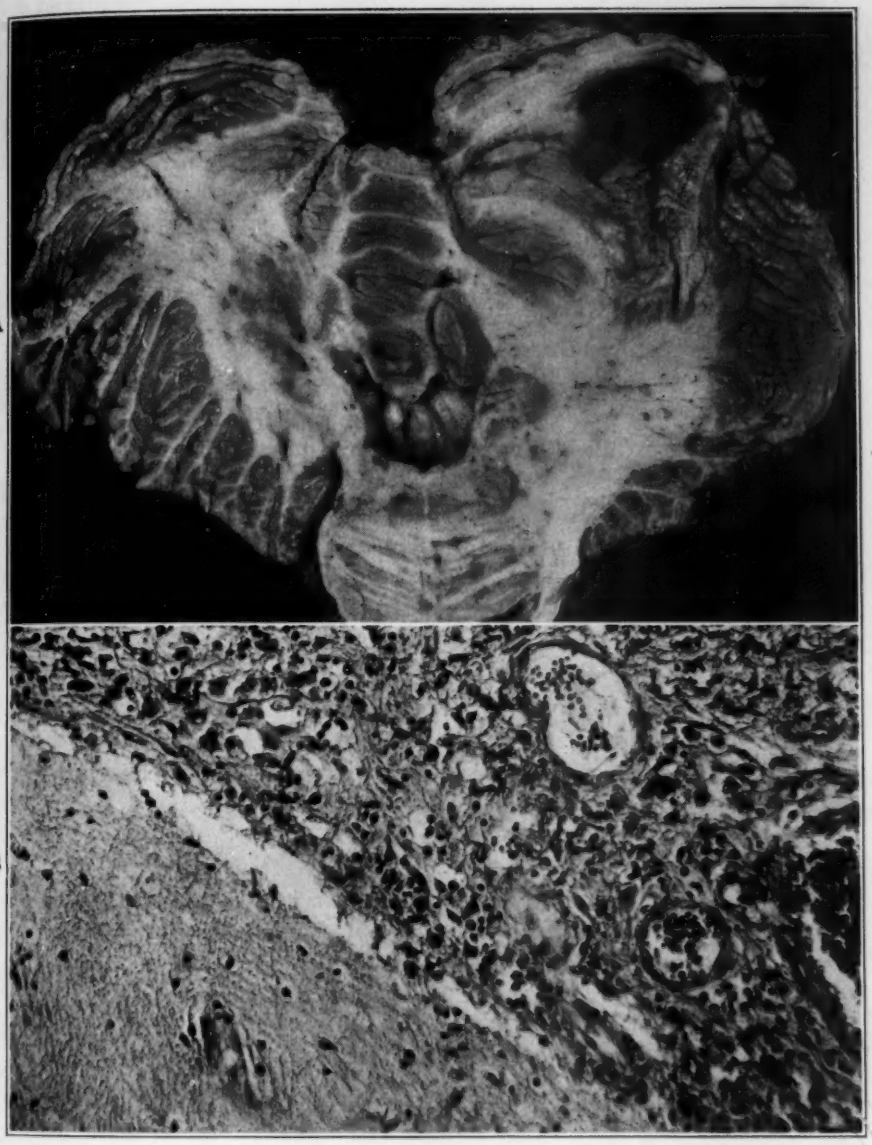


Fig. 24.—(*A*) Gross appearance of a hemangio-endotheliomatous (pial) meningioma and (*B*) histologic appearance of a hemangio-endotheliomatous (pial) meningioma (× 200).

tumor recalls the structure of the so-called hemangio-endothelioma. While the transition from the adjacent brain tissue to the tumor is sharp, there is, nevertheless, no line of separation or cleavage. The primitive vascular endothelium (fig. 24 *B*) is seen at the point of transition between the neoplasm and the brain tissue. In the deeper parts are seen areas containing numerous, still solid capillary sprouts and many wide, thin-walled channels (fig. 25 *A*). Then in other parts cells not unlike those seen in the mesenchymatous variety of meningioma and large cells rich in nuclear material, as noted in type IV, dominate the histologic picture (fig. 25 *B*). It would seem as though an attempt on the part of the cellular elements of the tissue to duplicate pial structures fell short of giving rise to more mature vascular structures and resulted in a primitive vascular design and structure recalling that of sarcoma.

However, in another subtype, the hemangiomatous variety, more mature vessels, such as are observed the pia, have formed in overabundance, though most of them are in the process of degeneration (fig. 26 *A* and *B*). Another example in which maturity of the blood vessels is reached and the tumor consists of little else than vessels of small caliber, many of which are hyalinized, can be seen in figure 27. At times such a tumor may contain little more than wide, thin-walled vascular channels and, hence, assumes the character of a cavernoma (fig. 28).

A third subtype, the so-called psammomatous variety, is characterized by abundance of psammoma bodies. Much thought has been given to the question of the origin of these bodies, commonly seen in meningeal tumor. From the days of Virchow, who for a time considered almost all types of meningioma as psammoma, the origin of the psammoma bodies and the rôle they play in the meningeal tumor were perplexing questions. There is, however, every reason to believe that the psammoma bodies are nothing but vascular buds ending blindly, thus blocking free circulation of the enclosed blood. The result is that the stagnant blood, as well as the enclosing vascular wall, undergoes degeneration, hyalinization and calcification (figs. 29 and 30). The same probably holds true for the psammoma bodies which are seen in various stages of degeneration in the normal meninges. They are frequently observed, as already demonstrated in figure 5 *B*, in small arachnoid remnants, where the little vascular buds, having been engulfed in foreign territory and not having been able to make contact with other vascular channels, become obliterated and form psammoma bodies. Essentially then, they are pial structures which stray during the formative stages into the arachnoid and dura and are cut off from the pia. The presence of psammoma bodies in the arachnoid or the dura

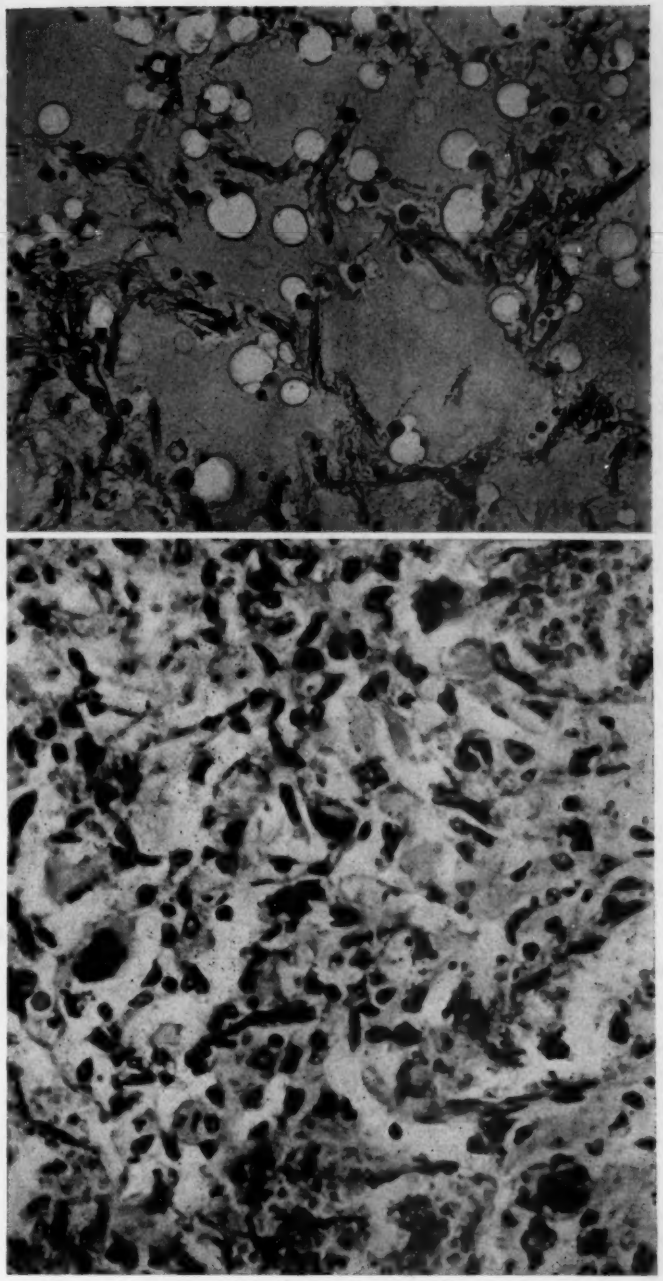
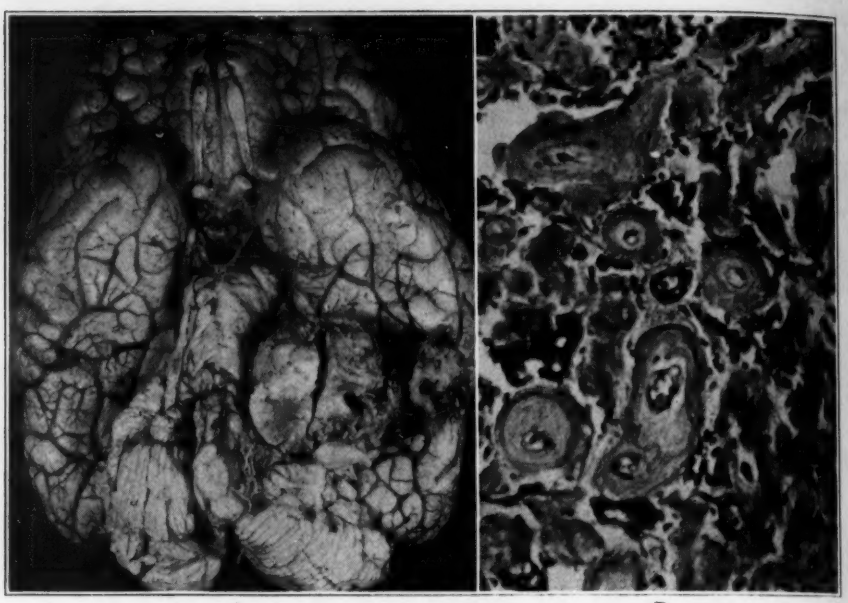


Fig. 25.—(*A*) Sinusoid in a hemangio-endotheliomatous pial meningioma (× 200) and (*B*) sarcomatous orientation of a pial meningioma (giant cells) (× 460).



A B

Fig. 26.—Appearance of a pial meningioma, simulating grossly an acoustic neurinoma and (*B*) histologic structure of hemangiomatous pial meningioma (× 280).

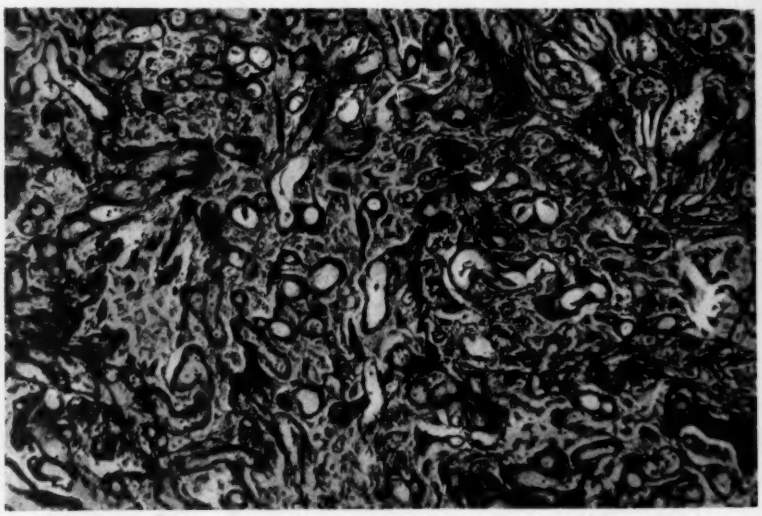
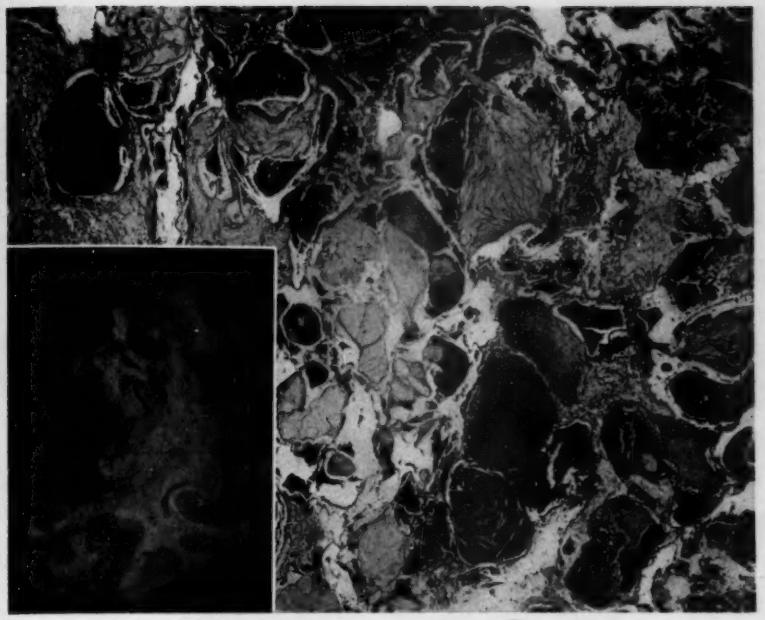
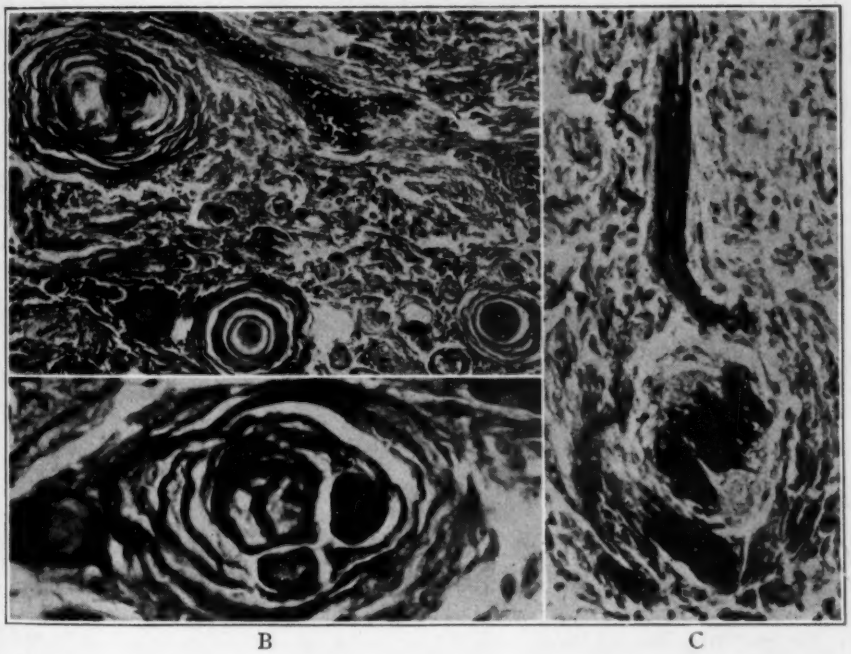


Fig. 27.—Histologic structure of hemangiomatous pial meningioma (× 120).



A B

Fig. 28.—(*A*) Gross appearance of a hemangiomatous pial meningioma, with the histologic structure of cavernoma (*B*) (× 12).



A

B C

Fig. 29.—Psammoma bodies seen in various formations. (*A*) Numerous, partially obliterated, degenerating blood vessels, of variable size, some of which have acquired the structure of typical psammoma bodies (× 200). (*B*) Higher magnification (× 640) of a large psammoma body, showing its internal structure. Compare with figure 30 *B-B*. (*C*) Sagittal section of a psammoma body (× 400). Compare with figure 30 *A-A*.

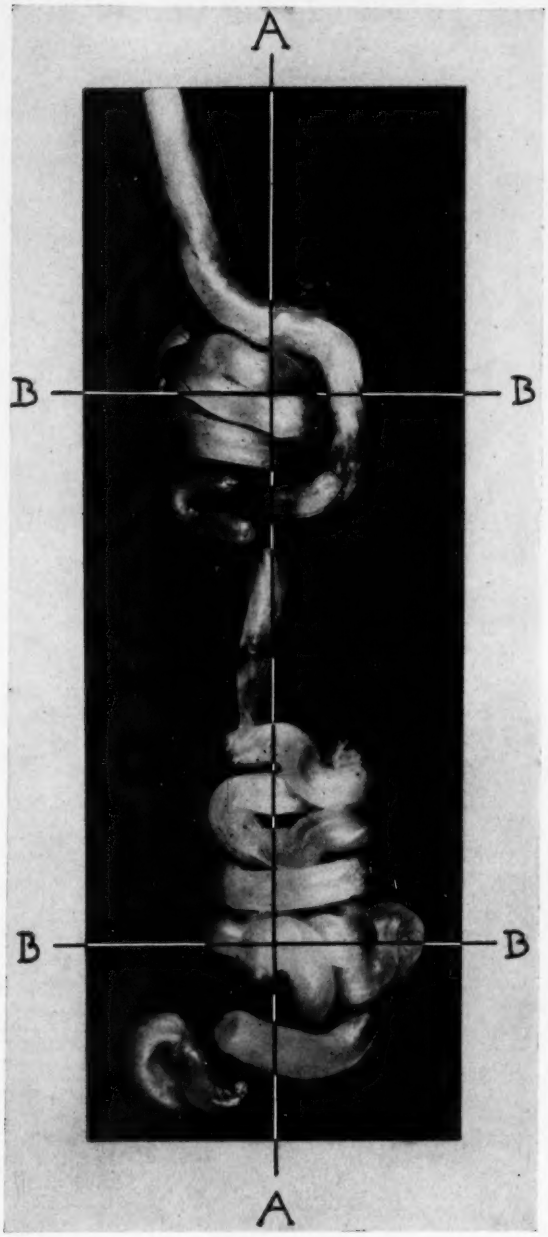


Fig. 30.—Approximate reconstruction of some of the vessels in the tumor shown in figure 29, illustrating the probable formation of psammoma bodies. The reconstruction was made with the aid of serial sections projected on cardboard (× 288). Line *A-A* indicates a sagittal section of this vessel, the probable appearance of which is given in figure 29 *C*. Line *B-B* indicates a cross-section of the vessel, the probable structure of which is shown in figure 29 *B*.

(fig. 17 *B*) may be regarded as further proof that at one time primitive dural, pial and arachnoid derivatives have gone astray and, having lodged in foreign territory, have undergone either degeneration or neoplastic formation.

Of the pial meningiomas the melanomatous variety may be regarded as another, though rare, subtype (Farnell and Globus[25]). Since melanin-bearing cells are frequent in the normal meninges, it should theoretically be possible to see these cells contributing in some degree toward the structure of a tumor derived from the meninges. This does occur, but in most instances such cells play a subordinate rôle. Occasionally they overshadow the other components and justify the acceptance of the view that a tumor primarily melanoblastic is to be grouped with the meningeal neoplasms (fig. 31). More commonly, however, the melanin cells are associated with other cellular elements of pial or arachnoid derivation (fig. 32).

RELATIONSHIP OF PIAL MENINGIOMA TO SARCOMA

Tumors of the varieties described theoretically may assume and practically do acquire at times a malignant character, and since the large majority are mesodermal in origin, the designation "sarcomatous" may be adopted. However, since the type of cell which is most capable of assuming a sarcomatous character is one which is nearest in type to vascular endothelium, most malignant meningeal tumors will be found to be allied to the tumor derived from the pia. Often in its gross appearance it is indistinguishable from the more quiescent meningioma, but histologic studies will disclose its meningeal origin and sarcomatous character (fig. 33 *A* and *B*). Since the pia is the meningeal membrane which penetrates the substance of the brain with the cerebral vessels and permeates the neuro-ectodermal tissue as a widely spread reticular network, it is conceivable that poorly differentiated and potent meningeal cells, having filtered into the brain with blood vessels, should serve as the source of primary sarcoma of the brain.

The sarcomatous meningioma, particularly when the term embraces all intracranial sarcomatous tumors of "leptomeningeal origin," is not as rare as Bailey[26] suggested. It still constitutes a relatively small percentage in published statistics on tumors of the brain, but this is due to the fact that it is as yet not fully recognized. Moreover, it is also likely that primary sarcoma of the brain and its meninges is often erroneously classified with malignant glioma (spongioblastoma or

25. Farnell, F., and Globus, J. H.: Primary Melanoblastosis of the Leptomeninges and Brain, Arch. Neurol. & Psychiat. **25**:803 (April) 1931.

26. Bailey, P.: Intracranial Sarcomatous Tumors of Leptomeningeal Origin, Arch. Surg. **18**:1359 (April) 1929.

glioblastoma), owing to the lack of thorough histologic investigation with modern staining methods or because of too much stress on a few stray glial elements among cell types of distinctly connective tissue variety, considered to be reactive in origin.

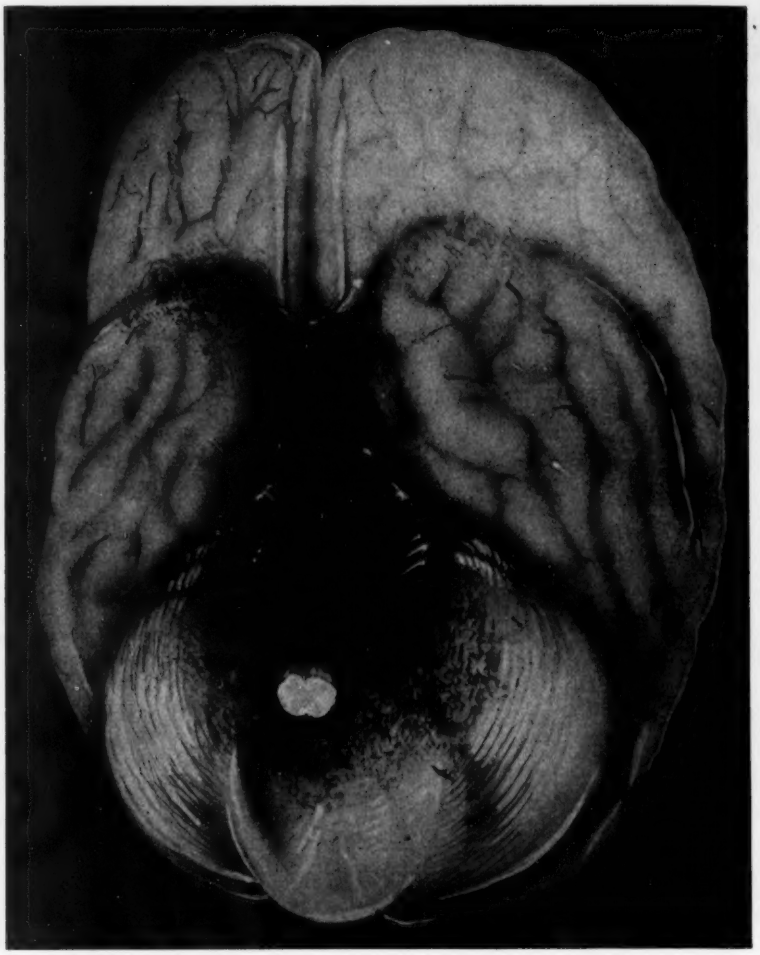


Fig. 31.—Gross appearance of a pial melanoblastic meningioma.

RELATIONSHIP OF MENINGIOMA TO MEDULLOBLASTOMA

The question as to the origin of the so-called medulloblastoma [27] is not entirely clear. The diagnosis is usually made on the location in

27. Cushing, H., and Bailey, P.: Tumors Arising from the Blood Vessels of the Brain: Angiomatous Malformations and Hemangioblastomas, Springfield, Ill., Charles C. Thomas, Publisher, 1928.

the midline, a fairly distinctive cellular organization (pseudorosette formation) and the presumably low resistance to roentgen ray therapy. However, many of these tumors fail to yield clearcut evidence of their gliogenous or neuroblastic character when special stains are utilized.

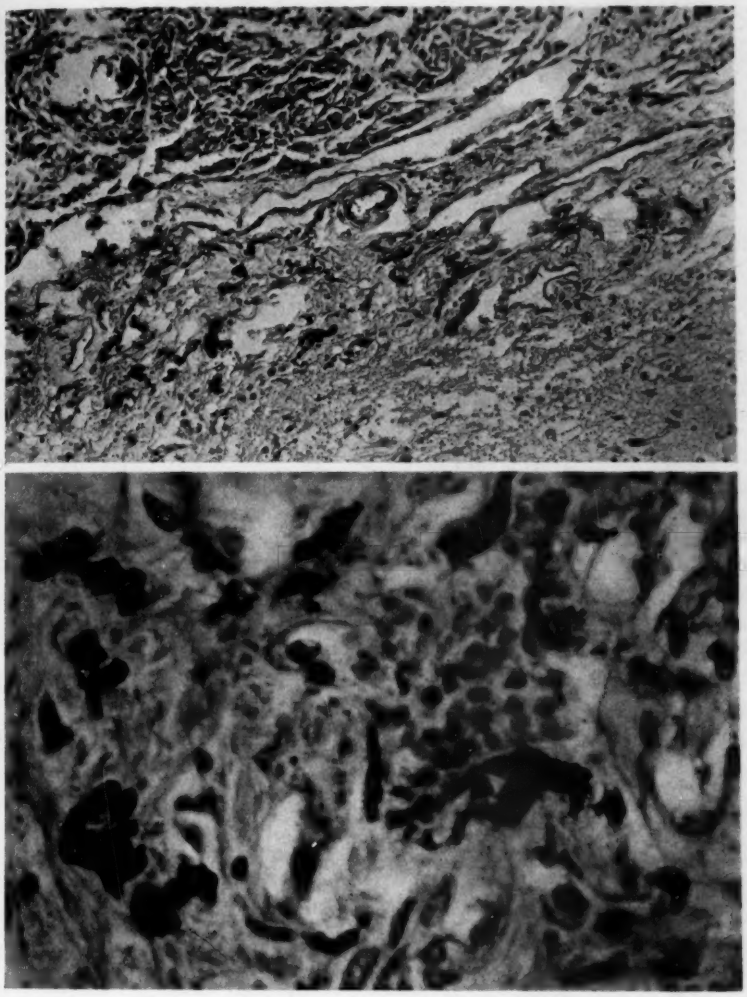


Fig. 32.—Pial meningioma with melanoblastic tendencies. (*A*) Low magnification (× 120) and (*B*) higher magnification (× 640).

On the other hand, if the tumor is studied carefully, areas may be observed in which vascular formations are dominant structural features (fig. 34). It is probable that restudy of some of these tumors and careful search for hemangiomatous structures would lead to the recog-

nition that at least in some instances the growth is a meningioma of pial variety in which the tumor found access to the interior of the cerebellum or took origin there from extensions of pial tissue. Silver and

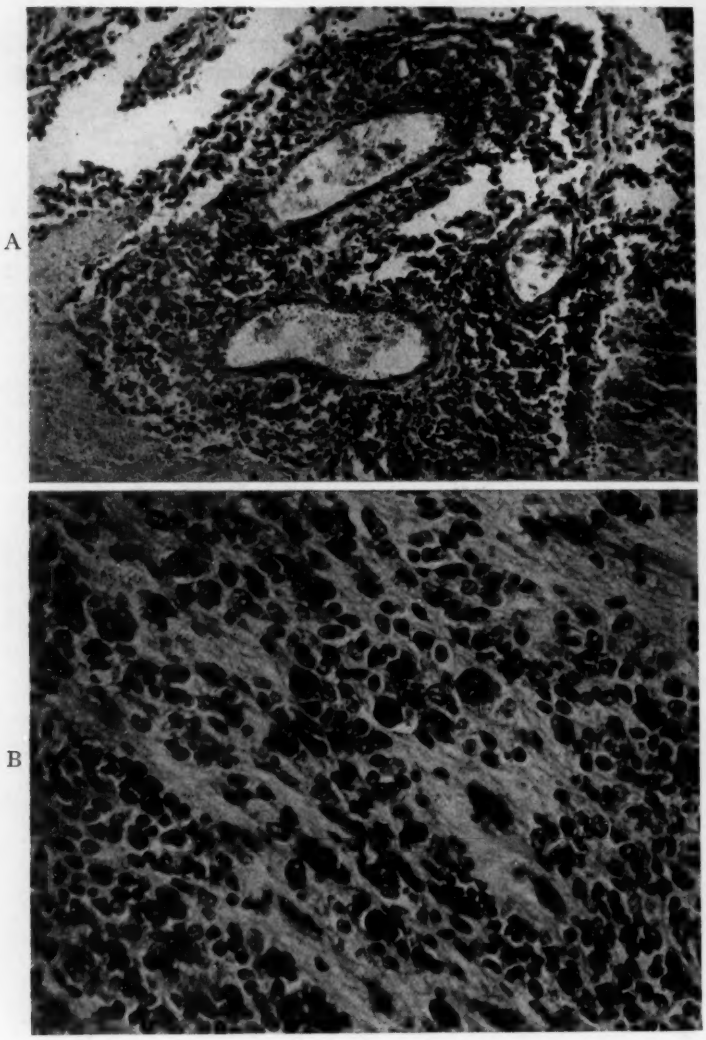


Fig. 33.—Histologic structure of sarcomatous meningioma. (*A*) Section of the tumor (× 100) and (*B*) section of a recurrent central sarcoma (× 250).

gold stains fail to establish the neuro-ectodermal origin of the dominant cell forms. The few glial cells or nerve cells that are occasionally observed in such a tumor may have strayed from adjacent brain tissue and need not be considered as determining the origin of the tumor in question.

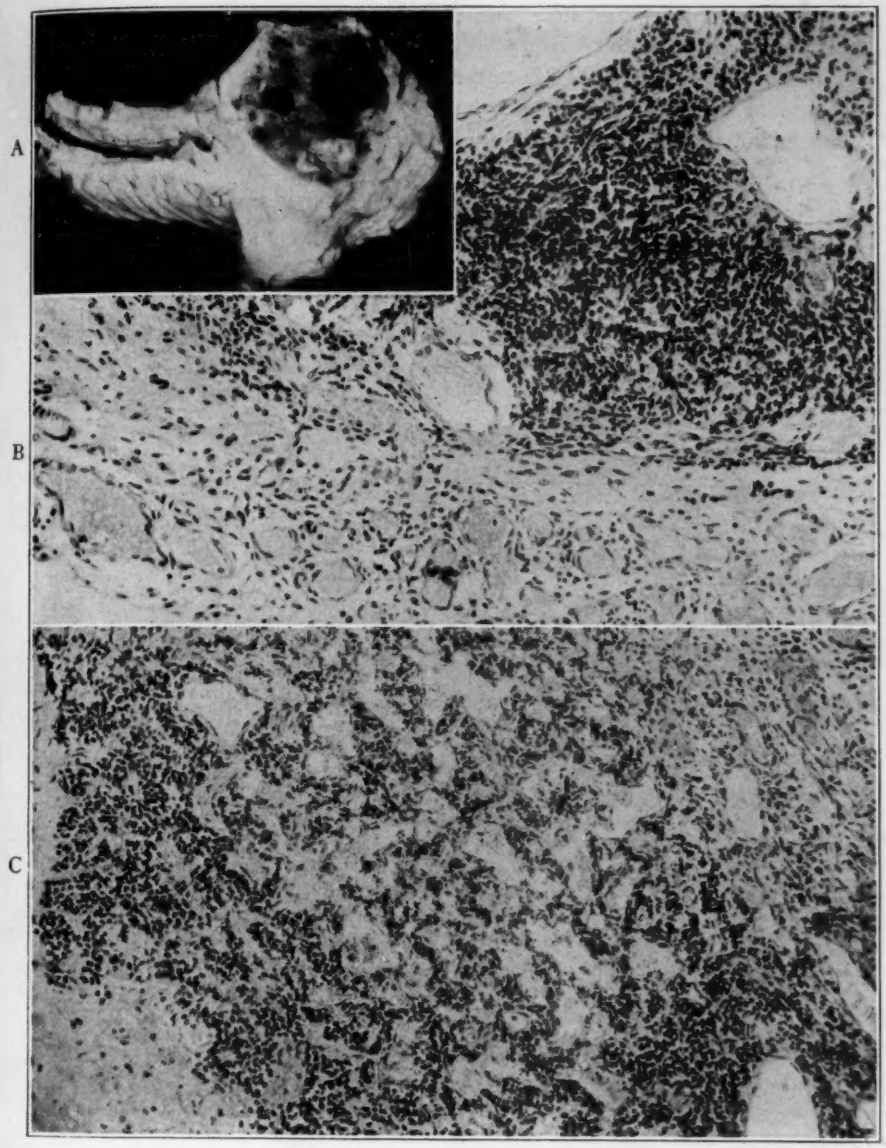


Fig. 34.—Pial meningioma simulating a medulloblastoma. (*A*) Gross appearance of pial hemangiomatous meningioma of the cerebellum, (*B*) histologic appearance of the tumor near the periphery (× 150) and (*C*) internal structure of a tumor simulating medulloblastoma (× 120).

Grossly, it is difficult to separate the so-called medulloblastoma from many other malignant and vascular neoplasms of the brain (fig. 34 *A*). Histologically, it shows the mosaic cell arrangement, with the cells grouped about vascular channels (fig. 34 *B*) in the form of pseudo-rosettes. Not infrequently there can be observed areas in which groups of capillaries and larger vessels border on cellular aggregations, in a manner not unlike that seen in the meningioma.

CLASSIFICATION OF MENINGIOMAS

The preceding considerations suggest the following classification of meningeal tumors (fig. 35):

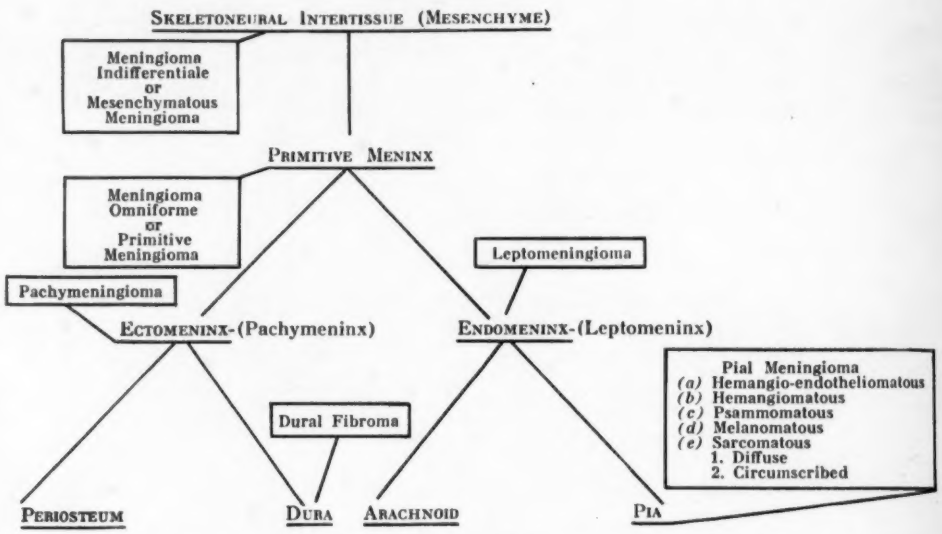


Fig. 35.—Chart showing a classification of meningeal tumors.

1. *Meningioma indifferentiale, or mesenchymatous meningioma.*

This tumor duplicates the structure of the mesenchymatous anlage of the meninges.

2. *Meningioma omniforme, or primitive meningioma.*

This tumor duplicates all the structures derived from the primitive meninx, which is already in an advanced stage of differentiation. It may contain bone traceable to the periosteal component of the "skeleto-neural intertissue," fibrous tissue recalling the structure of the dura, "epithelial" cells duplicating the cells in the arachnoid and vascular channels in various stages of maturation, denoting a pial origin.

3. *Meningioma pachymeningeale, or dural fibroblastoma.*

This type contains large, interlacing bundles of collagenous fibers, occasionally enveloping solid groups of cells of the epithelial variety.

This type of tumor, in which the dura alone is represented, is exceedingly rare. It may in areas present nothing but dural tissue, but on careful search arachnoid structures will be observed, and possibly some which indicate pial origin. Here remnants of bone are often prominent.

4. *Meningioma leptomeningeale, or arachnoid meningioma.*

In this type of tumor arachnoid structure predominates—not, however, to the full exclusion of the pial derivatives.

5. *Meningioma piale; pial or vascular meningioma.*

Here vascular structures of various types dominate the histologic picture, and, in accordance with the degree of maturity and the character of the vascular elements, the pial meningioma is divisible into several subgroups, such as the hemangio-endotheliomatous, the hemangiomatous and the psammomatous subtypes. Occasionally the pial tumor contains many pigment-carrying cells, acquiring a melanomatous character; this constitutes another subtype.

6. *Sarcomatous meningioma.*

This type of tumor, which cannot be distinguished from sarcoma elsewhere, is closely related by origin and structure to the mesenchymatous and pial forms of meningioma. It assumes the character of either diffuse meningeal sarcomatosis or circumscribed intracerebral sarcoma.

SUMMARY AND CONCLUSIONS

This study, which is based on a large number of meningeal tumors [28] of somewhat divergent structure, has been undertaken in an attempt to trace their respective forms to the probable source of origin and to explain their variation in structure. Since in the meninges the histogenetic factors are too obscure and unreliable to be useful for the solution of this problem, attention has been directed to the phylogenetic and ontogenetic processes which take place in the course of the development of the meninges. This method of approach was found to be useful and dependable, since little conflict exists in the opinions of investigators with regard to these processes. It is agreed that a mesenchymal tissue which fills the space between the skin and the neuro-ectoderm and is intimately connected, on the one hand, with the overlying skin and, on

28. The study is based on a histologic investigation of one hundred and three meningeal tumors, of which forty-six were obtained at autopsy and fifty-seven were made available after surgical intervention.

Hematoxylin and eosin, the Van Gieson stain, scarlet red, the Globus modification of the Cajal gold sublimate and the Hortega silver carbonate methods, Mallory's aniline blue and phosphotungstic acid stain, Weigert's elastica stain, Maximow's azur-eosin and the Holzer stain for glia were emphasized.

Many sections of the tumors used in this study were cut and stained by Dr. Abraham Blau.

the other, with the medullary tube is the early forerunner of all the brain coverings. It is also agreed that various processes of cleavage and fusion take place at various times in lower vertebrates and in man and that, in spite of the slight variation in the process of cleavage and fusion, one fact remains unchallenged: At one time the vascular pia, with its extensions to the brain substance, the arachnoid, the dura and the periosteum were all fused into one mesenchymal layer.

The tumor of meningeal origin is known at times to contain bone, collagenous connective tissue, endothelial cells and blood vessels, in different amounts and various stages of differentiation. The coexistence of all these tissues in the same tumor is readily explained by the fact that the undifferentiated meningeal primordium contains the ingredients essential for the elaboration of all these components. It is also clear that, while in some tumors the several constituents, reduplicating all the primitive parts of the meninges, may coexist in more or less equal amounts, in others they may occur in different ratios. Thus, in some the dural component may predominate, in some the pial and in others the arachnoid. However, in practically all tumors of meningeal derivation there is a preponderance of tissue elements with vascular orientation, and in a great number this orientation takes so decided a direction as to give the neoplasm an outspoken hemangiomatous character. Not infrequently the meningeal tumor, no matter where located in the brain, bears a strong resemblance to the cerebellar hemangioblastoma of Lindau.[29] The vascularity, the general pattern and the frequent occurrence of "foam cells" in both tumor forms point to their close relationship.

In spite of the existence of outspoken types of meningioma, it should be stressed that there is no sharp histologic demarcation between the mesenchymatous meningioma, on the one hand, and the pial forms, on the other, since between the extremes there are many transitions, with vague, almost undetectable, delimitations. Moreover, the cellular elements in many of these tumors, particularly those which are predominantly vascular, may undergo sarcomatous changes and thereby give rise to the more malignant tumor, in the form of diffuse or circumscribed sarcoma of the brain and its coverings. In some instances melanin-carrying cells contribute to the histologic picture.

It is obvious, therefore, that many variations in the cellular composition of this tumor are possible and occur without, however, contradicting their common derivation from the primitive meninx. There

29. Lindau, A.: Studien über Kleinhirncysten: Bau, Pathogenese und Beziehungen zur Angiomatosis retinae, Acta path. et microbiol. Scandinav., supp. 1, 1926, p. 1.

is also reason to believe that in some cases a tumor which has been described as a medulloblastoma is a pial meningioma, with a somewhat different organization. Similarly, it is obvious that the tumor of Lindau is little more than a hemangio-endotheliomatous variety of meningioma. The "foam cells" characteristic of the last-named variety and observed in almost all leptomeningeal tumors, particularly in the areas of "liquefaction," are not without biologic significance. They are not just morphologic anomalies but probably mark an attempt by tumor tissue to reduplicate a physio-anatomic step operative in the process of cleavage of the primitive meninges.

The occurrence of the giant cells frequently seen in the more vascular variety of the meningioma may be considered to be evidence of vigorous cell growth rather than, as has been suggested, a manifestation of degeneration. They are seen in the more cellular form of the meningioma and establish a link between the meningioma of the more quiescent type and that acquiring a sarcomatous character.

The origin of so-called hyperostosis, which, according to Cushing,[30] is associated with 25 per cent of the meningiomas, has puzzled many, but it is readily understood when the close relationship of the periosteum to the primitive meninges, the tissue presumably responsible for the neoplasm, is recalled. It is now recognized that this so-called hyperostosis is not a mere reaction to the underlying meningioma nor the result of some other independent factor (trauma) but that it is part of the neoplastic process, the tumor cells invading the haversian system of the overlying bone. Penfield, in discussing hyperostosis in relation to meningioma,[31] made the following significant statement:

> The connective tissue of the dura or bone may have proliferated and grown along with the tumor to assume the function of osteogenesis in this slowly growing neoplasm. On the other hand, the cells of the endothelioma may have acted as osteoblasts, changing somewhat in appearance during bone formation. As was mentioned (above), the arachnoid has been observed to contain bone (Cushing and Weed[32]) and the dura is said to serve as the periosteum.

Penfield then questioned his own views, by saying:

> But if bone is formed by cells derived from the tumor, it is difficult to understand why the intracranial portion of the endothelioma, which is likewise slow in growth, should not form bone also.

30. Cushing, H.: The Cranial Hyperostoses Produced by Meningeal Endotheliomas, Arch. Neurol. & Psychiat. **8**:139 (Aug.) 1922.

31. Penfield, W.: Cranial and Intracranial Endotheliomata, Hemicraniosis, Surg., Gynec. & Obst. **36**:657, 1923.

32. Cushing, H., and Weed, L. H.: Studies on the Cerebro-Spinal Fluid and Its Pathway: IX. Calcareous and Osseous Deposits in the Arachnoidea, Bull. Johns Hopkins Hosp. **26**:367, 1915.

Nevertheless, his views expressed in the opening part of his statement are in almost complete accord with my own observations.

It is necessary also to correct at this point a statement made frequently (Cushing,[12] Mallory[10] and Penfield[33]) that the meningioma never passes beyond the pial barrier and never penetrates the brain. In the larger number of the tumors investigated in this study, the tumor had invaded the brain tissue to variable depths. Similarly, adhesions between the tumor and the dura are not infrequent. They, too, are due to the common origin of the dura and the tissues from which the tumor is formed rather than to incidental passage of vessels, as claimed by some investigators.

The generic term meningioma is accepted in preference to the other names. The term "arachnoid fibroblastoma," which is now in vogue, is rejected, since it is somewhat misleading by implying the unconditionally benign character of this tumor. A simplified classification of the meningiomas is offered. It is based on the identification of each variety with some dominant cell form and cell organization which characterizes a stage in the development of the meninges.

1133 Fifth Avenue.

33. Penfield, W.: Principles of the Pathology of Neurosurgery, in Nelson New Loose-Leaf Surgery, New York, Thomas Nelson & Sons, 1932, vol. 2, p. 1932.

PATHOLOGIC FEATURES OF MULTIPLE SCLEROSIS AND ALLIED CONDITIONS

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Notwithstanding the wealth of contributions to knowledge of the pathologic picture and pathogenesis of multiple sclerosis, the status of these problems seems to be at present more confused than ever. Thus, aside from the classic form of multiple sclerosis, there are seriously considered acute, subacute, malignant and experimental forms, while some authors have included with this morbid condition disseminated encephalomyelitis, Schilder's disease, postvaccinal and postmeasles encephalitis, Binswanger's subcortical chronic encephalitis, neuroptic myelitis and what Bassoe and I [1] described as multiple degenerative softening. Another extreme is represented by authors, Spiller,[2] for instance, who described multiple sclerosis as merely a form of disseminated encephalomyelitis. The main reason for such confusion is the tendency to regard multiple sclerosis as a conglomeration of sclerotic plaques and to identify them with patches of so-called demyelinization. Since patches of demyelinated nerve fibers are present not only in multiple sclerosis but in many other diseases of the nervous system, some investigators are inclined to group such diseases as variants of multiple sclerosis—acute, transitional and other types. Putnam and his co-workers [3] even went so far as to speak of experimental multiple sclerosis, regardless of the fact that nature has not produced multiple sclerosis in animals and that the pathologic features as described "in the experimental form" differ from those seen in the human type.

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1. Hassin, George B., and Bassoe, Peter: Multiple Degenerative Softening Versus Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:613 (May) 1922.

2. Spiller, William: Encephalomyelitis Disseminata, Tr. Am. Neurol. A. **55**:62, 1929.

3. Putnam, Tracy J.; McKenna, John B., and Evans, Joseph: Experimental Multiple Sclerosis in Dogs from Injection of Tetanus Toxin, J. f. Psychol. u. Neurol. **44**:460 (May) 1932. Putnam, Tracy J.; McKenna, John B., and Morrison, L. R.: Studies in Multiple Sclerosis: I. The Histogenesis of Experimental Sclerotic Plaques and Their Relation to Multiple Sclerosis, J. A. M. A. **97**:1591 (Nov. 28) 1931.

The pathologic characteristic of multiple sclerosis [4] may be summed up as chronic progressive degeneration of the central nerve fibers and spinal roots (especially the posterior) and, according to some authors, even of the peripheral nerves. The degeneration of the nerve fibers appears in all its phases, initial and late. The initial phases exhibit swelling of the myelin sheaths, their progressive breaking up and transformation into lipoids, through the activity of the glia. It is possible in cases of multiple sclerosis to trace the various stages of myelin degeneration—from excessive formation of Elzholz bodies, myeloclasts and Marchi globules to that of myelophages, various forms of fat granule bodies (gitter cells) harboring destroyed nerve tissue transformed into lipoids and the ultimate formation of a glial scar. The destruction of the parenchyma—first of the myelin and later of the axon—provokes parallel reactive phenomena in the glia, the blood vessels and the meninges. The glia cells (oligodendrocytes and cytoplasmic astrocytes) proliferate, giving rise to a variety of phagocytic formations; the adventitia of the blood vessels becomes hyperplastic and thickened and may affect slightly the size of the lumen, which, however, does not become occluded by blood clots or organized thrombi. I have never seen hemorrhages or the accumulation of blood pigment in cases of pure, uncomplicated multiple sclerosis, though, like engorgement of the veins, they may be agonal and consequently should not be considered characteristic. There are no changes in the intima or the elastic membrane, nor is there infiltration of the adventitial tunic with hematogenous cells. Infiltrations involve the Virchow-Robin spaces, the infiltrating cells being usually fat granule bodies (gitter cells). Occasionally these cells are mixed with lymphocytes and plasma cells. As the gitter cells are ultimately discharged into the subarachnoid space, the adventitial spaces occupied by them collapse, and the adventitia appears thickened, homogeneous and hyperplastic; the lymphocytes and plasma cells may remain the sole contents of the adventitial spaces and thus suggest an inflammatory condition. The inflammation is especially well evidenced in the cerebral subarachnoid space, where the lymphocytes and plasma cells are mixed with gitter cells, which have come from the adventitial spaces of Virchow and Robin.[4] Their presence in the adventitial spaces or in the subarachnoid space acts as a foreign body, which, like any foreign body, provokes a reaction (symptomatic inflammation, according to Spielmeyer) in the form of an accumulation of lymphocytes or plasma cells. The latter process is thus a secondary change, as has already been emphasized by

4. Hassin, George B.: Studies in the Pathology and Pathogenesis of Multiple Sclerosis, Arch. Neurol. & Psychiat. **7**:589 (May) 1922.

Dawson.[5] Numerous as the last two types of cells may be in cases of multiple sclerosis, they are never as striking and widespread as in association with inflammatory conditions of the brain or the cord (poliomyelitis, epidemic encephalitis, disseminated encephalomyelitis, encephalitis following typhus, dementia paralytica, rabies and other typical infections of the central nervous system). In multiple sclerosis such inflammatory infiltrations, if present, are overshadowed by the masses of degenerative products, which on superficial examination of improperly stained sections appear to a careless and prejudiced observer as inflammation. When one contrasts the changes observed in the aforementioned inflammatory lesions of the central nervous system with those in multiple sclerosis, one cannot escape the conviction that the pathologic pictures in the two groups are not identical. Yet, as has been stated, several authors did not hesitate to include multiple sclerosis with the inflammatory group of nerve disorders and considered it not a specific morbid entity but an encephalomyelitis.

As vast areas of demyelinization occur in association with postvaccinal encephalomyelitis, this morbid condition is also identified with the acute form of multiple sclerosis. However, there are many differences between the postvaccinal form of encephalomyelitis and multiple sclerosis. Thus, in multiple sclerosis the destruction of the axis-cylinders is comparatively late. The process follows the degeneration of the myelin but may also early exhibit tumefaction and other slight morphologic changes, whereas in postvaccinal encephalitis the axons become more or less affected simultaneously with the myelin. In multiple sclerosis the nerve degeneration is accompanied by a manifest and virile glial reaction; in postvaccinal encephalitis the reaction is not glial but microglial (mesodermal). The perivascular infiltrations in multiple sclerosis are intra-adventitial and composed chiefly of fat granule bodies; in postvaccinal encephalitis they are mainly extra-adventitial and consist for the most part of microglial cells. The blood vessels in multiple sclerosis exhibit no regressive changes and remain patent, in spite of the hyperplasia of the adventitial tunic; in postvaccinal encephalitis the blood vessels, especially the veins, are always engorged and may even be thrombosed. The oligodendroglia is never swollen in multiple sclerosis but is definitely so in postvaccinal encephalitis. The simultaneous destruction of the myelin and the axons, the prevalence of the microglial reaction and the vast extra-adventitial destruction of the nerve parenchyma have also been described in cases of postmeasles encepha-

5. Dawson, James W.: (*a*) The Histology of Disseminated Sclerosis, Edinburgh M. J. **17**:229, 1916; (*b*) Rev. Neurol. & Psychiat. **15**:94, 1917; (*c*) **16**:296, 1917.

litis.[6] It is possible that in both postvaccinal and postmeasles encephalitis the noxious agent, though it affects the parenchyma primarily, as in multiple sclerosis, is of a different nature. On the basis of the extent and intensity of the nerve changes, the process in these morbid conditions is not slow, as is that in multiple sclerosis, which may last for years, but is rapid and generally much more destructive.

In the usual inflammatory, infectious type of encephalomyelitis the phenomena are inflammatory and overshadow the degenerative changes, which generally are meager. The difference in the reactive phenomena associated with multiple sclerosis, disseminated (infectious, infiltrative) encephalomyelitis and postvaccinal (toxic) encephalitis is due not to the time element—the acuteness or chronicity of the morbid process—but to specific histologic changes, which stamp these diseases as separate morbid entities. To consider postvaccinal encephalitis or disseminated encephalomyelitis as forms of acute multiple sclerosis is not proper, as there is no such morbid entity as acute multiple sclerosis. Multiple sclerosis is always a chronic disease process, regardless of the time when the clinical picture becomes manifest. As the disease may be latent and show no signs or symptoms, as during remissions, it is not to be wondered that a patient may not feel sick for a long time and yet may harbor the disease. The condition may become manifest rather acutely, from accidental causes, such as trauma, psychic factors, infection or intoxication. When the so-called acute form is studied histologically, one observes the same type of changes seen in the classic chronic type. Acute, subacute, mild or atypical as multiple sclerosis may be, recovery from this disease is not possible, but recovery is possible from what are termed the acute forms—disseminated encephalomyelitis and postvaccinal encephalitis. This fact alone should speak against the identity of the three morbid entities.

The fundamental feature of multiple sclerosis is that the changes are not confined to the plaques but are diffuse and scattered throughout the entire central nervous system; that is, even areas apparently normal exhibit histologic changes. These can be followed well in specimens prepared with the nuclear stains, such as thionine and toluidine blue and even hematoxylin and eosin. The area seen in figure 1 *B*, for instance, is a portion of a densely cellular patch covering the gray matter and the lateral and part of the posterior column. The blood vessels are distended and infiltrated with gitter cells; oligodendrocytes are scattered among them and outside the blood vessels. The areas adjacent to the patch are less densely infiltrated than the plaques, while the remote areas appear

6. Ferraro, Armando, and Scheffer, I. H.: Encephalitis and Encephalomyelitis in Measles: A Pathologic Report of Six Cases, Arch. Neurol. & Psychiat. **25:** 748 (April) 1931.

normal under low power. However, under higher power one can discern in such apparently normal areas, by mere counting, an increase in the number of cells (fig. 2 *B*) and, among the latter, cell elements which in the corresponding area of a normal cord are sparse or absent. Among such cells one may note rod cells and sometimes cytoplasmic astrocytes, while the myelin and axis-cylinders, when properly stained with the methods of Marchi or of Alzheimer and Mann or with the combined stain-

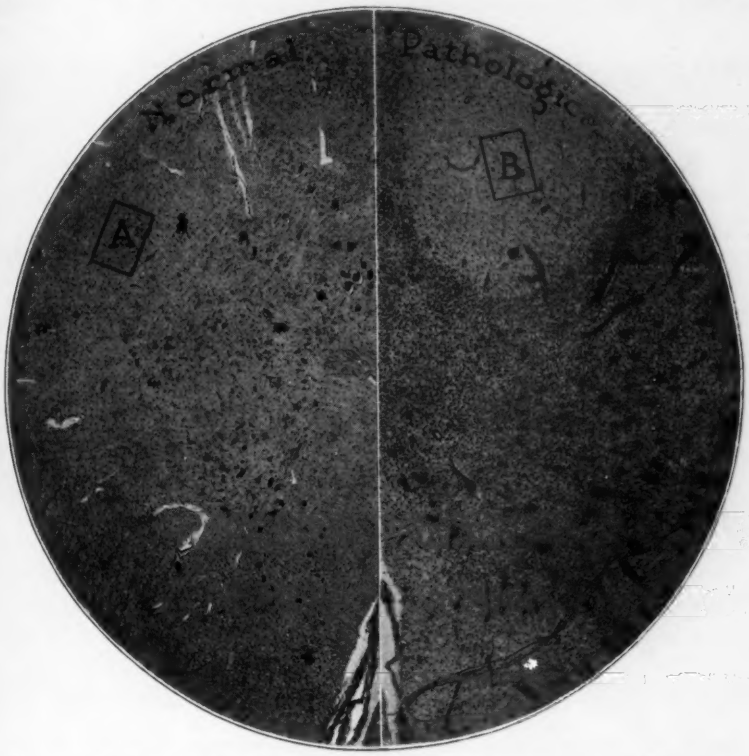

Fig. 1.—At the left is shown half of a normal cord, devoid of the extensive infiltrations in the gray matter and anterolateral column appearing in the photomicrograph at the right, of a cord from a patient with multiple sclerosis. The areas *A* and *B* are of normal appearance and are reproduced with higher magnification in figure 2.

ing methods, are swollen and show an increase in the number of Elzholz bodies. On the whole, a patch of multiple sclerosis exhibits nothing typical, for patches of sclerotic nerve tissue containing stray axons occur also in a great variety of other degenerative nerve diseases (tabes, Friedreich's ataxia, sclerotic atrophy of the cerebellum [7] and other con-

7. Hassin, George B.: Sclerotic Atrophy of the Cerebellum, Arch. Neurol. & Psychiat. **31**:1205 (June) 1934.

ditions). As such they are of little, if any, help in attempts to evaluate the type of changes involved in multiple sclerosis, however detailed and vivid their description may be. Being a terminal phase of nerve degeneration, a patch is devoid of specific features, and for this reason one is not justified in forming conclusions pertaining to the pathologic features and pathogenesis of multiple sclerosis from histologic studies of the plaques of sclerosis. As a fact, such studies may be misleading, especially when one relies too much on the staining method of Weigert

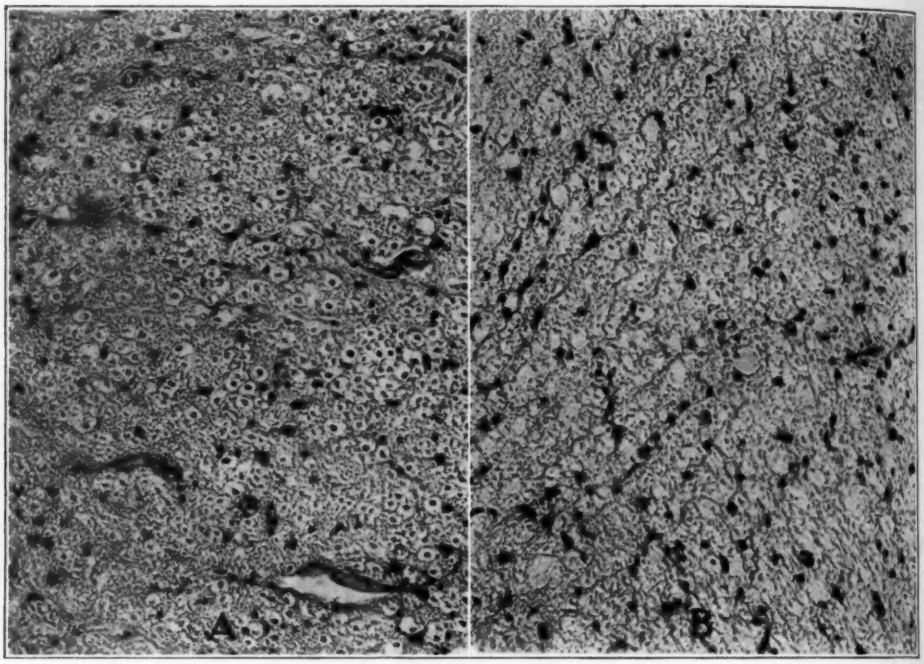

Fig. 2.—Photomicrographs with higher magnification of the areas *A* and *B* indicated in figure 1. *A* shows an area from a normal cord, *B*, a corresponding area in the cord of a patient with multiple sclerosis. Not only are the nuclei more numerous in *B*, but the contour of the myelin and the axons is much less distinct than in the section (*A*) from a normal cord.

and Pal or its modifications. These methods help only to determine the site and extent of the lesion, whereas the methods of nuclear staining bring out such important features as the diffuseness of the changes and the extensive glial reaction, not only in the vicinity of the plaques but in remote areas. With the use of additional staining methods (such as the Alzheimer-Mann technic) it is also possible, as has been said, to demonstrate the widespread swelling of the myelin, which, it must be emphasized again, is the primary process, followed by reactive changes in

the glia, the walls of the blood vessels and the meninges, and the ultimate formation of plaques of sclerosis—all of which are secondary phenomena. The diffuseness of the process precludes its dependence on the vascular blood supply, and this, of course, pertains also to its ultimate phase—the patches. Elsewhere,[4] I have pointed out that "the patch does not follow the course of a blood vessel," as Dawson and others have shown. Dawson, for instance, studied small foci of sclerosis serially throughout their whole extent and came to the conclusion that they do not coincide with the vascular areas at all. Symonds [8] stated, for unexplained reasons, that I erroneously quoted Dawson. To settle this point, I shall quote Dawson verbatim and shall not merely refer to him, as in the previous contribution.[4] Dawson stated:

> In the course of this study several small areas have been followed up, serially, throughout their whole extent, and I have come to the conviction that the changes appear within, but do not coincide with, the area of distribution of the arteries (page 126).[5b]

The attempt of Putnam [9] to invoke venous thrombosis as the cause of the sclerotic patches does not help to clarify the situation, for the patches, as has been pointed out, are the terminal and not the essential pathologic manifestations. Since they are exceedingly numerous and are always preceded by diffuse myelin changes, the patches should then be associated with immense masses of thrombi, which the patient would carry for decades, without signs of apparent circulatory disturbance in the brain or the spinal cord. Though venous thrombi may occur in association with acute or septic inflammatory conditions, they are not known to exist in cases of uncomplicated multiple sclerosis. Dawson,[5] for instance, observed only aggregations of white cells in the vessels of the cord and the presence of fibrin, which, he said, have been taken as an indication of intravital thrombosis. Nowhere, however, has evidence been present of the organization of such thrombi or of alterations in the walls of the vessels in relation to them, nor have these thrombi always been related to sclerotic areas. Nor are arterial thrombi known in pure forms of the disease, easy as it is to locate them because of the parenchymatous changes produced by them. What the parenchymatous changes caused by venous thrombi are is not known. Putnam injected oily substances into the ligated superior longitudinal sinus of dogs and concluded that "plaques were produced." He studied the plaques and

8. Symonds, C. P.: Pathological Anatomy of Disseminated Sclerosis, Brain **47**:36, 1924.

9. Putnam, Tracy J.: The Pathogenesis of Multiple Sclerosis: A Possible Vascular Factor, New England J. Med. **209**:786 (Oct. 19) 1933; The Biological Significance of the Lesions of Multiple Sclerosis, Science **80**:295 (Sept. 28) 1934.

thrombi so produced in paraffin sections stained with the method of Masson, which stains practically everything, including the plasma of the blood. In one case Putnam observed platelets, but he did not state whether or not the condition was complicated by septic, terminal or other changes. Obstruction of the longitudinal sinus does not cause retrograde hyperemia or patches. At least in my case [10] of an organized thrombus of the superior longitudinal sinus, which was of sixteen months' duration and, thus, was much older than the thrombi in Putnam's experiments, such changes were not present. The changes showed as light, scattered areas in the brain which did not take the stain. They appeared rarefied and broken up, contained no blood vessels and showed no signs of organized thrombi. In short, congestion of the blood vessels, hemorrhages or other vascular changes may occur in association with multiple sclerosis, but only as agonal or accidental phenomena and not as its cause. The only essential change in multiple sclerosis is primary degeneration of the nerve fibers. It is primary because it is independent of the condition not only of the blood vessels but of the ganglion cells. In advanced stages the ganglion cells of the brain and the spinal cord may show changes, but neither clinically nor pathologically do they play any rôle in multiple sclerosis.

That degeneration of central nerve fibers may be produced primarily by toxins (tetanus, carbon monoxide, potassium cyanide, dysentery toxin and guanidine) and exhibit degenerative changes resembling those seen in multiple sclerosis may be gathered from numerous experiments by Claude,[11] Ferraro,[12] Putnam and his co-workers [3] and, especially, Lotmar.[13] Lotmar produced changes in the central nervous system in rabbits by injecting dysentery toxin. The animals were kept alive for from fifteen hours to twenty-one days, and the changes in the nervous system were observed to vary according to the dose of the toxic substance injected, the duration of its action, the age and resistance of the animal and other factors. Some changes were mild; others were severe, when they were associated with marked destruction of the ganglion cells and ameboid transformation of the glia cells. In mild forms there were

10. Hassin, George B.: Abscess and Thrombosis of the Superior Longitudinal Sinus: Clinicopathologic Report of a Case, Arch. Neurol. & Psychiat. **29**:359 (Feb.) 1933.

11. Claude, H.: Myélite expérimentale subaiguë par intoxication tétanique, Arch. de physiol. norm. et path. **9**:843, 1897.

12. Ferraro, Armando: Experimental Toxic Encephalomyelopathy, Psychiatric Quart. **7**:267 (April) 1933.

13. Lotmar, Fritz: Beiträge zur Histologie der akuten Myelitis und Enzephalitis, sowie verwandter Prozesse, auf Grund von Versuchen mit Dysenterietoxin, in Nissl, F., and Alzheimer, A.: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fisher, 1913, vol. 6, no. 2.

swelling of the myelin and proliferation of the glia, with formation of gitter cells but no lymphocytic infiltration, though the adventitial and the endothelial cells appeared proliferated. The glia reacted only in cases of mild involvement, when the dose used was moderate and the animals could be kept alive longer than seven days. When the dose injected was large or the resistance was low, the animal usually succumbed in less than seven days. A remarkable feature was that some experimental animals simultaneously exhibited both the severe and the mild type of glial reaction. Thus, some areas presented regressive glial changes of the type of ameboid glial cells, but in the neighboring areas there were also progressive changes in the glia, in the form of its considerable proliferation. Lotmar observed no thrombi in the numerous small foci of nerve destruction. Many features described by Lotmar—the diffuse changes in the myelin (tumefaction) with the subsequent degeneration of the axon, the secondary glial reaction with formation of gitter cells, the absence of inflammatory changes in the blood vessels and the good general condition of the animal—resemble the changes seen in association with multiple sclerosis. The differences between the changes shown in Lotmar's animals and those in multiple sclerosis are the simultaneous involvement of the gray matter (especially when large doses were injected) in the animals, which sometimes was affected even more than the white substance, and their excellent condition after suspension of the injection of mild doses. In cases of multiple sclerosis the patient is in good health only during remissions, and as the invasion of the body by toxins in this disease is continuous and apparently never stops until death, the morbid process never regresses. In the diffuseness of the pathologic process, the selective destruction of the myelin and the progressive course of the disease with occasional remissions lie the essential features of multiple sclerosis. That some of the aforementioned changes may be traced to the action of a toxin was thus definitely established by the elaborate experiments of Lotmar, in which the nature, the dosage and the duration of the action of the toxin were definitely known. They are so far not known in connection with multiple sclerosis or other toxic conditions (neuroptic myelitis and Schilder's disease), while in the postvaccinal or the postmeasles type of encephalitis the real nature of the toxin, although it can only be surmised, is certainly different from that of the problematic toxins of multiple sclerosis. It must also differ in a morbid entity which Bassoe and I describe as multiple degenerative softening.[1] The latter disease comprises a large number of rather indefinite clinical pictures, with acute or subacute course, often associated with elevation in temperature and usually with a definite history of infection or intoxication. Large patches of demyelinization are numerous in the pons and elsewhere in the brain but sparse in the medulla and the spinal cord. The patches

consist of degenerated nerve tissue, mainly the white substance, with an abundant collection of gitter cells in the perivascular spaces of Virchow and Robin. In the capillaries the gitter cells are the only infiltrating cells, but in the larger vessels they are mixed with lymphocytes and some plasma cells. There are changes also in the ganglion cells but none in the blood vessels, and signs of formation of a glial scar are absent; that is, the patches are not sclerotic, as in multiple sclerosis, but consist of nerve fibers that either become softened and transformed into lipoids or are in the process of less advanced degeneration, with a mild glial reaction. The patches are not ischemic; that is, they are not caused by a vascular disturbance (such as thrombosis), for the reactive phenomena in ischemic foci are mesodermal and not glial. It is possible, as has been emphasized elsewhere,[1] that some indefinite clinical syndromes described as acute or malignant multiple sclerosis, degenerative encephalitis and disseminated encephalomyelitis are variants not of multiple sclerosis but of multiple degenerative softening. Cases of such conditions are not uncommon but unfortunately are misinterpreted and are, for this reason, misleading. As an illustration, I shall cite the case of Symonds.[8]

A woman aged 38 complained of paresthesias (first in the upper and later in the lower extremities and around the waist) and weakness of the left upper extremity. There was improvement of two months' duration, followed by ptosis of the left eye, which also disappeared in a few weeks. Several months later the weakness in the left arm recurred and was accompanied by disturbances of speech and gait and slight paralysis of the left facial nerve. The condition progressed, and examination about one year after the onset of the disease revealed dysarthria, dysphagia, paralysis of the third, sixth and seventh nerves on the left, weakness of the extremities with incoordination (of the upper extremities), disturbances of the sphincters, absence of the majority of the abdominal reflexes and a Babinski sign on the left. An interesting feature was an unaccountable "low" pyrexia of several weeks' duration. The patient once more improved considerably and had been well the "whole summer," but in the "late autumn" paresthesias, symptoms of bulbar involvement and sphincter troubles reappeared. The patient died, after an illness of about two years. Necropsy revealed numerous patches (minute and large) around the fourth ventricle and the sylvian aqueduct and in the brain and rather few patches in the spinal cord. The blood vessels were engorged; some were thrombosed, and many were infiltrated with "mononuclear" cells. Some vessels were infiltrated only with lymphocytes and others only with fat granule bodies, and in many blood vessels "perivascular cuffing with lymphocytes and the so-called fat granule myelitis were apparent side by side." In the spinal cord the "earliest and primary" change appeared to be "an increase both in the number and the thickness of the glia fibrils which run parallel with the myelinated nerve fibers," with relatively little formation of astrocytes, which was a striking reactive feature at an early stage of myelin degeneration in the brain. The degeneration was confined to the myelin sheath, and the patches or foci were observed in all stages, from that of "acute fatty degeneration to that of the dense gliosis of the true sclerotic patch."

Aside from the "primary increase in the number and thickness of the glial fibrils" (which is hard to understand, as the increase in multiple sclerosis is not primary but secondary), the changes as outlined by Symonds correspond with what Lotmar described in his experiments as a mixed type of glial reaction and with what may also occur in cases of multiple degenerative softening. Neither clinically nor pathologically (if one judges from the illustrations) was the case cited one of multiple sclerosis, and it cannot be utilized, as Symonds tried to do, for demonstrating the type and nature of changes that occur in multiple sclerosis.

Like multiple sclerosis, multiple degenerative softening is a specific morbid entity, and this name should be substituted for such improper and meaningless terms as acute, subacute or malignant multiple sclerosis. Its cause is toxic factors which attack the nerve fibers directly, without the intermediation of vascular factors (endarteritis, embolism, thrombosis, arteriosclerosis and other changes), and produce definite changes, such as softening due to ischemia or anoxemia. The histologic differences between vascular and degenerative softening are: In vascular softening both the parenchyma and the glia perish; the reaction is mesodermal, and the duration, like the onset, is acute. In degenerative softening the parenchyma is mainly affected, and only in cases of exceptionally severe involvement does the glia also undergo degeneration, the course and onset being gradual or subacute. With postvaccinal encephalitis, neuroptic myelitis [14] and Schilder's disease multiple degenerative softening forms a separate group of subacute parenchymatous nerve disorders, which differ from one another (and also from multiple sclerosis) clinically and pathologically. Though they possess a common feature, the areas of demyelinization, they are nevertheless distinct morbid entities—as are poliomyelitis, epidemic encephalitis, encephalitis following typhus and dementia paralytica, which are recognized specific morbid entities, though they also possess a common feature, perivascular infiltration. As each member of the second group is thought to be due to a specific infection, so each member of the first group is probably due to a specific intoxication. It is true that the exact nature and name of the toxins in the majority of the toxic states are not known, but neither is the exact nature of some infectious diseases (such as smallpox, rabies and poliomyelitis); yet they are universally classified as such.

CONCLUSIONS

1. Patches or plaques are not the essential feature of multiple sclerosis but merely one of its phases, a terminal condition.

2. The essential feature of multiple sclerosis is diffuseness of the degenerative process, which in the early stages occurs as foci of demyelinization.

14. Hassin, George B.: Neuroptic Myelitis Versus Multiple Sclerosis: A Pathologic Study, Arch. Neurol. & Psychiat. **37**:1083 (May) 1937.

3. The nuclear staining methods (such as toluidine blue) bring out the extent of the microscopic changes much better than any other method and should be widely used.

4. Blood vessels play no rôle in the genesis of the changes in multiple sclerosis, in which the nerve fibers are attacked primarily and directly, without the intermediation of the blood vessels.

5. In addition to multiple sclerosis, a morbid entity—multiple softening—should be considered, usually described as acute or malignant multiple sclerosis.

A PROPOSED MECHANISM OF EMOTION

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The work of Cannon,[1] Bard,[2] Penfield,[3] Ranson[4] and others has greatly advanced knowledge of the functions of the hypothalamus. In the light of these researches the connections of the hypothalamus to the medial wall of the cerebral cortex gain a new significance. The following discussion presents some anatomic, clinical and experimental data dealing with the hypothalamus, the gyrus cinguli, the hippocampus and their interconnections. Taken as a whole, this ensemble of structures is proposed as representing theoretically the anatomic basis of the emotions.

It is generally recognized that in the brain of lower vertebrates the medial wall of the cerebral hemisphere is connected anatomically and integrated physiologically with the hypothalamus and that the lateral wall is similarly related to the dorsal thalamus (Herrick[5]). These fundamental relations are not only retained but greatly elaborated in the mammalian brain by the further development of the hippocampal formation and the gyrus cinguli in the medial wall and of the general cortex in the lateral wall of each cerebral hemisphere.

The main steps in the phyletic history of these structures are clearly represented in the various classes of vertebrates. It is not surprising, therefore, to find that the literature on this fascinating subject presents on the whole a congruent account. Step by step, the structures of the medial wall become differentiated into the hippocampal formation, which

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1. Cannon, W. B.: The James-Lange Theory of Emotion: A Critical Examination and an Alternative Theory, Am. J. Psychol. **39**:10-124, 1927; Again the James-Lange and the Thalamic Theories of Emotion, Psychol. Rev. **38**:281-295, 1931.

2. Bard, P.: (*a*) The Central Representation of the Sympathetic Nervous System as Indicated by Certain Physiologic Observations, Arch. Neurol. & Psychiat. **22**:230-246 (Aug.) 1929; (*b*) Emotion: I. The Neuro-Humoral Basis of Emotional Reactions, in Murchison, C. A.: A Handbook of General Experimental Psychology, Worcester, Mass., Clark University Press, 1934, chap. 6, pp. 264-311.

3. Penfield, W.: Wesley M. Carpenter Lecture: Influence of the Diencephalon and Hypophysis upon General Autonomic Function, Bull. New York Acad. Med. **9**:613-637, 1933; Canad. M. A. J. **30**:589-598, 1934.

4. Ranson, S. W.: The Hypothalamus: Its Significance for Visceral Innervation and Emotional Expression, Tr. Coll. Physicians Philadelphia **2**:222-242, 1934.

5. Herrick, C. J.: Morphogenesis of the Brain, J. Morphol. **54**:233-258 (March 5) 1933.

establishes the first efferent connection of the cortex, namely, the fornix, with the hypothalamus, and as the adjacent cingular cortex appears, it receives, per contra, an afferent connection from the hypothalamus. Step by step, the lateral wall above the pyriform cortex becomes differentiated into the lateral nonolfactory cortex, which through the medium of the internal capsule maintains its afferent and recurrent connections with the nuclei of the dorsal thalamus. The histories of the two walls of the hemispheres owe their disparity and distinctive structure to two totally different kinds of integration—the hippocampus and the cingular cortex participating in hypothalamic activities and the lateral cortex in the general sensory activities mediated by the dorsal thalamus. It is also noteworthy that in both systems two way connections exist between the cortical and the thalamic level.

The account which follows will be concerned chiefly with the reciprocal connections which exist between the hypothalamus and the gyrus cinguli and hippocampus. Its chief purpose is to point out that these connections may mediate by means of the cortical circuit the important function commonly called emotion.

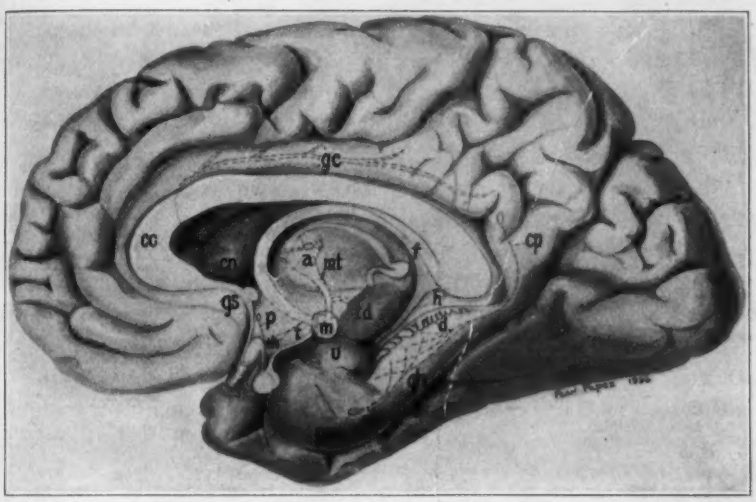
The term "emotion" as commonly used implies two conditions: a way of acting and a way of feeling. The former is designated as emotional expression; the latter, as emotional experience or subjective feeling. The experiments of Bard [2a] have demonstrated that emotional expression depends on the integrative action of the hypothalamus rather than on that of the dorsal thalamus or cortex, since it may occur when the cerebral hemispheres and the dorsal thalamus are totally removed. For subjective emotional experience, however, the participation of the cortex is essential. Emotional expression and emotional experience may in the human subject be dissociated phenomena. Hence, emotion as a subjective state must be referred to the higher psychic level. Concerning the theory of emotion based on diencephalic processes, Bard [2b] wrote:

> As we have seen, every relevant experimental fact points away from the periphery and directly toward the brain as the site of the processes which determine whether or not a stimulus shall give rise to emotional feeling. What is the nature and the locus of these all-important central processes?
>
> Cannon [1] (1927, 1931) and also Dana [6] (1921) have proposed the theory that emotion results from the action and reaction of the cerebral cortex and the diencephalon. This theory, unlike the James-Lange theory, has considerable experimental support and takes into account anatomical and physiological facts ignored by the older view. First of all, there is the evidence that at the base of the diencephalon are located the neural patterns responsible for emotional behavior, mechanisms capable of independent discharge but normally held in check by the cerebral cortex. At the same time the cerebral cortex is the immediate site of emotional consciousness, and, as we have seen, emotional experience and emotional

6. Dana, C. L.: The Anatomic Seat of the Emotions: A Discussion of the James-Lange Theory, Arch. Neurol. & Psychiat. **6**:634-639 (Dec.) 1921.

expression may be dissociated by disease or surgical intervention. But we know that thalamic processes are a source of affective experience, that bodily sensations such as are sometimes associated with emotion may be thalamic in origin. Well-established anatomical facts show that, with the possible exception of the olfactory, all sensory impulses are interrupted at the thalamic level before gaining the cerebral cortex, and Head's (1920) studies suggest how there may be regrouping of corticopetal impulses in the thalamus. Cannon's theory has its basis in these facts and it proposes that, at the same time that the diencephalon discharges downward the motor impulses which produce the emotional behavior, it discharges upward to the cortex impulses which throw into action the processes which underlie emotional consciousness.

In order to make clear at the outset the general anatomic picture which I wish to propose as the probable corticothalamic mechanism of emotion,



Medial view of the right cerebral hemisphere, showing the hippocampus and its connection with the mamillary body through the fornix and also the connections of the mamillary body to the anterior thalamic nuclei and thence to the cortex of the gyrus cinguli. In this specimen an unusually large exposed (nude) hippocampus is seen.

Abbreviations

a, anterior nucleus
ab, angular bundle
cn, caudate nucleus
cc, corpus callosum
cp, cingulum posterius
d, gyrus dentatus
f, fornix
gc, gyrus cinguli
gh, gyrus hippocampi
gs, gyrus subcallosus
h, hippocampus nudus
m, mamillary body
mt, mamillothalamic tract
p, pars optica hypothalami
pr, pyriform area
sb, subcallosal bundle
t, tuber cinereum
td, tractus mamillotegmentalis
th, tractus hypophyseus
u, uncus

a diagram has been constructed, showing its main features (figure). I shall start with the hypothalamus, the three parts of which are illustrated. The pars optica is connected through the infundibulum with the pars neuralis of the hypophysis. The tuber cinereum is connected downward with the lower sympathetic centers. In the human brain a large tract can be seen passing down, ventral to the red nucleus. The pars mamillaris is connected in an efferent way to the cortex of the gyrus cinguli. The pars mamillaris also receives afferent connections from several other sources, the most prominent being the fornix from the hippocampal formation.

As the figure shows, it is the mamillary body which bears the main hypothalamic relations to the cerebral cortex. This is a two way connection in the nature of a circuit through the cerebral cortex, at the upper level, and through the mamillary body, at the hypothalamic level. In this circuit impulses may be incited at two points: the cerebral cortex and the hypothalamus. Incitations of cortical origin would pass first to the hippocampal formation and then down by way of the fornix to the mamillary body. From this they would pass upward through the mamillothalamic tract, or the fasciculus of Vicq d'Azyr, to the anterior nuclei of the thalamus and thence by the medial thalamocortical radiation (in the cingulum) to the cortex of the gyrus cinguli.

The central emotive process of cortical origin may then be conceived as being built up in the hippocampal formation and as being transferred to the mamillary body and thence through the anterior thalamic nuclei to the cortex of the gyrus cinguli. The cortex of the cingular gyrus may be looked on as the receptive region for the experiencing of emotion as the result of impulses coming from the hypothalamic region, in the same way as the area striata is considered the receptive cortex for photic excitations coming from the retina. Radiation of the emotive process from the gyrus cinguli to other regions in the cerebral cortex would add emotional coloring to psychic processes occurring elsewhere. This circuit would explain how emotion may arise in two ways: as a result of psychic activity and as a consequence of hypothalamic activity.

The hypothalamus is accessible to both visceral and somatic sensory impressions from many peripheral sources, and it is well known that emotional coloring, or affect, may be associated with all sorts of sensory experiences of bodily and receptor origin. Most of the afferent receptor systems evoke sensations with characteristic qualities, perceptions, etc., which at the conscious level are accompanied by a more or less distinctive affective tone. The question arises as to how these afferent sensibilities, which pass through the dorsal thalamus and then by way of the internal capsule to the cerebral cortex, are capable of acquiring emotional coloring. Physiologic results imply that the emotive process is mediated by

the hypothalamus, and anatomic data suggest that it is the mamillary body which sends the excitations to the cortex of the gyrus cinguli.

It has been aptly said that the hypothalamus is the recipient of the vague and undefined impressions from many bodily sources which in their totality represent afferent material capable of influencing the regulative functions of the hypothalamus. It is not yet generally recognized that there are primitive sensory centers in the ventral thalamus, the chief connections of which appear to pass to the hypothalamus. These primitive receptive centers in the ventral thalamus (subthalamus) are known as the pars ventralis of the lateral geniculate body, the nucleus praegeniculatus, the pars ventralis of the medial geniculate body, the reticular nucleus and the nucleus of the mamillary peduncle. These primitive centers receive certain terminals from various afferent systems: For example, the optic tract ends in part in the pregeniculate nucleus and in the pars ventralis of the lateral geniculate body; the acoustic system ends in part in the pars ventralis of the medial geniculate body; the spinothalamic and trigeminothalamic tracts end in part in the reticular nucleus, and the medial lemniscus appears to contribute fibers to the nucleus of the mamillary peduncle.

These nuclei of the ventral thalamus send to the hypothalamus diffuse fiber connections, some of which are better known as the supraoptic decussations. They end in general in the pars optica and the tuber cinereum, the regions which regulate visceral activities and emotional expression. However, the pars optica and the tuber are connected with the mamillary body, which also receives afferent connections through the medial bundle of the forebrain, the mamillary peduncle and the fornix. Thus, the mamillary body is the ultimate recipient of various afferent excitations, which reach the hypothalamus especially through the afferent centers of the ventral thalamus.

It is thus evident that the afferent pathways from the receptor organs split at the thalamic level into three routes, each conducting a stream of impulses of special importance. One route conducts impulses through the dorsal thalamus and the internal capsule to the corpus striatum. This route represents "the stream of movement." The second conducts impulses from the thalamus through the internal capsule to the lateral cerebral cortex. This route represents "the stream of thought." The third conducts a set of concomitant impulses through the ventral thalamus to the hypothalamus and by way of the mamillary body and the anterior thalamic nuclei to the gyrus cinguli, in the medial wall of the cerebral hemisphere. This route represents "the stream of feeling." In this way, the sensory excitations which reach the lateral cortex through the internal capsule receive their emotional coloring from the concurrent processes of hypothalamic origin which irradiate them from the gyrus cinguli.

The aim of the following discussion is to call attention to a number of anatomic regions and their connections, which taken as a whole may be regarded as an integrated mechanism. This, with the aid of clinical data, may be interpreted as subserving the physiologic emotive processes and the psychologic function of emotion itself.

THE HIPPOCAMPAL FORMATION

In an interesting essay, Lewis [7] has given an account of the history and significance of the term hippocampus, as applied to the cerebral structure first described in the human brain by Arantius, in 1587. Golgi,[8] in an excellent monograph described and illustrated the fine histologic structure of this region, including the pyramidal cells of the hippocampus and the small granule cells of the fascia dentata.

Ramón y Cajal,[9] in his unique studies of the histologic structure of the brain, gave an exhaustive and lucid description of the minute structure of the hippocampal formation and its fiber connections, which he included in the olfactory apparatus. Briefly, the main points are as follows: The central olfactory apparatus consists of (1) the olfactory bulb, which is the primary olfactory receptive center, (2) the pyriform (sphenoid) lobe, which is the center of the olfactory perception and (3) the hippocampal formation, which is an association center dealing with the retention and recall of olfactory impressions and their integration with the ideomotor processes of the brain in general. The olfactory nerve terminates in the olfactory bulb. The lateral olfactory tract carries the excitations to the pyriform cortex, terminating there in an external fiber stratum. The pyriform cortex, in particular its posterior part, the angular nucleus (centrum spheno-occipitale or *noyau angulaire*), gives origin to a tract of fibers, the angular bundle *(Winkelstrang oder sphenoammonische Bahn* or *faisceau angulaire ou temporo-ammonique),* which gains an internal position and follows the closed medial angle of the temporal horn of the lateral ventricle, adjacent to the hippocampus—hence its name, the angular bundle. The fibers of this bundle perforate the subiculum of the hippocampal gyrus (*perforierende Fasern* or *fibres perforantes)* and on its external surface form the substantia reticularis alba (Arnoldi), which enters the hippocampal fissure. Here they end in two ways. Part of them synapse with the dendrites of the granule cells of the gyrus dentatus (fascia dentata), and part enter the lacunar

7. Lewis, F. T.: The Significance of the Term Hippocampus, J. Comp. Neurol. **35**:213-230, 1923-1924.

8. Golgi, C.: Istologia normale, in Opera omnia, Milan, U. Hoepli, 1903, vol. 2, chap. 16, pp. 397-536; Sulla fina anatomia degli organi centrali del sistema nervoso, Riv. sper. di freniat. **9**:1-17, 1883.

9. Ramón y Cajal, S.: Die Riechrinde beim Menschen und Säugetier, in Studien ueber die Hirnrinde des Menschen, Leipzig, A. Barth, 1900, no. 4. Histologie du système nerveux de l'homme et des vertébrés, Paris, A. Maloine, 1909.

layer of the hippocampus. A portion of the angular bundle does not perforate on the same side but passes dorsally to cross in the hippocampal commissure and terminate in the hippocampal formation of the opposite side.

The view is generally held (Ariëns Kappers [10] and others) that the gyrus hippocampi and the fascia dentata are the receptive cortex for this region, while the pyramidal cells of the hippocampus major form the emissive, or motor, layer giving rise to the fornix, or the cortico-hypothalamic tract.

Ramón y Cajal also showed the intimate relation which exists between the posterior portion of the cingulum and the regions from which the angular bundle takes origin. This fiber connection was illustrated schematically by Dejerine (vol. 2, fig. 327),[11] showing the intimate relation which exists between the gyrus cinguli and the hippocampal formation. This bundle forms another connection of special interest in regard to the theory of hippocampal functions presented here.

In a mangabey monkey examined by me, from which Professor Dusser de Barenne had removed both temporal lobes, the subcallosal bundles were completely severed. Sections of this brain showed that the cingulum posterior is the largest bundle which enters the medullary core of the gyrus hippocampi. In addition, there was retrograde degeneration of a conspicuous system of association fibers passing from the gyrus cinguli to the temporal lobe. From the gyrus cinguli these fibers pass laterally and ventrally across the internal capsule. In this animal the presence of these degenerated fibers was an obtrusive feature. No previous record of them occurs in the literature.

The subcallosal fasciculus of Muratoff [12] is well known. It lies next the ependyma of the lateral ventricle in the angle formed between the corpus callosum and the caudate nucleus. In the dog and other mammals this bundle can be readily peeled away from the corpus callosum and the lateral wall of the ventricle, and thus its curved course can be traced into the temporal horn, into the region of the angular bundle adjacent to the hippocampal formation. Onufrowicz [13] first described this fiber stratum as the occipitofrontal fasciculus in the brain of a microcephalic idiot which possessed no corpus callosum to confuse the picture. Bechterew [14] stated that, according to Muratoff, the bundle

10. Ariëns Kappers, C. U.: The Development of the Cortex and the Function of Its Different Layers, Acta psychiat. et neurol. **3**:115-132, 1928.

11. Dejerine, J.: Anatomie des centres nerveux, Paris, J. Rueff, 1901.

12. Muratoff, W.: Sekundäre Degeneration nach Durchschneidung des Balkens, Neurol. Centralbl. **12**:316 and 714, 1893.

13. Onufrowicz, W.: Das balkenlose Mikrocephalengehirn Hofman, Arch. f. Psychiat. **18**:305-328, 1887.

14. Bechterew, W.: Les voies de conduction du cerveau et de la moelle, Lyon, A. Storck & Cie, 1900, p. 604.

degenerates after lesions of the frontal, parietal and occipital gyri. He stated that Shukowski's experiments on the frontal cortex and the gyrus cinguli (illustrated in Bechterew's [14] book) produced degeneration of this bundle, which was particularly profuse following lesions of the cortex of the gyrus cinguli.

Dejerine,[11] in numerous figures, has illustrated the subcallosal bundle as the *substance grise sous-épendymaire* lying between the caudate nucleus and the corpus callosum. In relation to his *substance grise sous-épendymaire,* he showed the occipitofrontal fasciculus of Forel and Onufrowicz as a special, well myelinated bundle, which extends into the wall of the temporal horn of the ventricle and forms there the tapetum of the sphenoid lobe. In his case,[15] Moriceau (page 148), it degenerated after a frontal lesion.

Mettler [16] (page 532) reviewed the literature and contributed his own observations that lesions of the prefrontal area produce degeneration of the descending and ventral parts of the subcallosal fasciculus. He made this observation:

> The posterior component continues backward in dorsal association with the caudate nucleus and makes the return loop with it (into the temporal pole) after sending some fibers to travel more posteriorly beneath the ependyma.

Bechterew and others expressed the belief that the polarity of the bundle is occipitofrontal and that it bears an intimate relation to the caudate nucleus. However, the experimental evidence strongly supports the opposite view that the origin of the subcallosal bundle is frontal, cingular and parietal and that it terminates in a medullary center in the gyrus hippocampi, close to the angular bundle. If this view is correct, the subcallosal bundle and its associated structures constitute another associational link between the general cortex and the hippocampal formation.

The general view of most morphologists, e. g., Ramón y Cajal, Dejerine, Turner and G. E. Smith, has been that the hippocampus, and even the entire limbic lobe, mediate in some obscure way the olfactory sector of functions. The angular bundle is, in fact, of olfactory origin, but it is not the only cource of hippocampal incitations. The cingulum posterius brings the cingular gyrus into relation with the hippocampus. Though less important, the subcallosal bundle, including the occipitofrontal fasciculus (tapetum), probably brings the prefrontal region and the gyrus cinguli into functional relation with the hippocampal formation. These make possible the interpretation that central processes from various parts of the cortex may incite hippocampal activity.

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15. Dejerine,[11] vol. 2, p. 148.

16. Mettler, F. A.: Cortifugal Fiber Connections of the Cortex of Macaca Mullatta: The Frontal Lobe, J. Comp. Neurol. **61**:509-542, 1935.

For centuries the functional significance of the hippocampus has remained unknown. The hippocampus is by no means a vestigial structure; it may vary greatly in development in different persons. Retzius,[17] commenting on this, stated that the varied development of the hippocampus is independent of age, sex or special prominence of any known psychic function. Ferrier [18] was the first to test the matter experimentally. He destroyed the hippocampus in monkeys and described the depressive effect it produced on cutaneous sensibilities. He expressed the belief that it is the center for these sensibilities. What seems more important now, he described a tendency to somnolence in stating that the monkey was continually tending to drop off to sleep. Subsequent observations have placed the zone of cutaneous sensibility in the parietal lobe, leaving the functions of the hippocampus in obscurity.

Since the Negri bodies, the essential lesions of rabies, or hydrophobia, have their site of predilection in the hippocampus and the cerebellum and since the disease is characterized by intense emotional, convulsive and paralytic symptoms, there seems to be offered an important clue to the probable location of the emotive mechanism. The prodromal symptoms—insomnia, irritability and restlessness—usher in the stage of excitement and profound emotional perturbation. There is extreme hyperesthesia to all forms of stimuli, such as light and sound, and every stimulus situation provokes great apprehensiveness and paroxysms of fear. The patient presents the appearance of intense fright and of mingled terror and rage. Hydrophobia, or fear of water, develops as a result of painful pharyngeal spasms when the patient attempts to swallow fluids. Foaming at the mouth is the common symptom of autonomic disturbance. The predominance of hypothalamic lesions in the supraoptic nucleus has been described by Nicolau and Kopciowska.[19] Wood [20] stated:

> The Negri bodies are, as a rule, most abundant in the large ganglion cells of the hippocampus major, but occur in ganglion cells of the cerebral cortex and elsewhere.

17. Retzius, G.: Das Menschenhirn, Stockholm, P. A. Norstedt & Söner, 1896, vol. 1, p. 67.

18. Ferrier, D.: The Functions of the Brain, London, Smith, Elder & Co., 1876.

19. Nicolau, S., and Kopciowska, L.: Rage du lapin, à virus fixe, et corps de Negri; dénombrement comparatif des inclusions dans la corne d'Ammon et dans la zone élective (noyau optique basal), Compt. rend. Soc. de biol. **112**:445-448 (Feb. 10) 1933; abstr., J. A. M. A. **100**:1190 (April 15) 1933.

20. Wood, F. C.: Delafield and Prudden's Text-Book of Pathology, ed. 16, Baltimore, William Wood & Company, 1936, p. 334.

Bassoe and Grinker [21] (fig. 13) stated that Negri bodies are demonstrable with ease in the ganglion cells of the cornu ammonis and the adjacent temporal lobe. However, they added:

> It is important to note that from the appearance of the ganglion cell containing the Negri bodies no more degenerative changes were associated with their presence than in the other ganglion cells.

From such evidence it is possible to construct the hypothesis that the hippocampus participates in some important way in the central production of the emotive process.

THE GYRUS CINGULI

The cortex which borders the corpus callosum on the medial side of each hemisphere is the gyrus cinguli, or the gyrus fornicatus. From the adjacent cortex it is sharply set off by the cingular sulcus. Posteriorly it broadens out into the precuneus, and around the splenium of the corpus callosum it merges with the hippocampal gyrus. Broca assigned the gyrus cinguli to the limbic lobe, and Turner included it in the rhinencephalon. However, as Edinger [22] (page 216) remarked, it is a question whether the gyrus cinguli belongs to the olfactory apparatus. Such a grouping, Berry [23] (page 341) said, is arbitrary and misleading, as it is not in accordance with either morphologic or functional fact.

The cyto-architecture of this gyrus has been described by Campbell [24] and Ramón y Cajal [9] and recently by von Economo and Koskinas [25] (plate 51). The relations of the fiber bundle, known as the cingulum, to the gyrus have been long recognized. This has been generally interpreted as an association bundle which, according to some authors, is connected with the septal and subcallosal region and, according to others, is more strongly connected to the precuneus and the hippocampal region, through the cingulum posterius.

It was Ramón y Cajal who intimated that the cingulum carries afferent fibers from some unknown source. The recent discovery of an

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21. Bassoe, P., and Grinker, R. R.: Human Rabies and Rabies Vaccine Encephalomyelitis: Clinicopathologic Study, Arch. Neurol. & Psychiat. **23**:1138-1160 (June) 1930.

22. Edinger, L.: The Anatomy of the Central Nervous System of Man and of Vertebrates in General, edited by W. S. Hall, Philadelphia, F. A. Davis Co., 1899.

23. Berry, R. J. A.: Brain and Mind, or the Nervous System of Man, New York, The Macmillan Company, 1928.

24. Campbell, A. W.: Histological Studies on the Localization of Cerebral Functions, Cambridge, University Press, 1905.

25. von Economo, C., and Koskinas, G. N.: Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen, Berlin, Julius Springer, 1925.

afferent thalamocortical connection from the anterior thalamic nuclei to the gyrus cinguli is to be credited to Clark and Boggon [26] and Waller.[27] These thalamic connections have been shown by the Marchi and the retrograde cell degeneration technics in the rat and cat. There are indications that in the brain of the monkey similar connections are present (Walker,[28] page 30). The course of these fibers has not been illustrated or described in detail. In general they pass laterally and forward from the anterior and anterodorsal nuclei to enter the anterior limb of the internal capsule. They turn dorsally and medially over the anterior horn of the ventricle to enter the cingulum, in the medial wall of the hemisphere. I have observed their degeneration in the rat after injury to the frontal lobe and after incision of the medial wall of the cortex. According to Clark and Boggon and Waller, the connections of the small anterodorsal nucleus are with a small area of cortex of the retrosplenial region, while the anterior nucleus is connected with the extent of the gyrus cinguli. These nuclei also have a strong connection through the inferior thalamic peduncle *(ansa peduncularis)* with the anterior part of the pallidum and by a strong triangular band which passes forward probably with the head of the caudate nucleus. In considering the anterior thalamic nuclei as centers in a functional system, connections with the corpus striatum, as well as with the cingular cortex, must be recognized.

So far as functions of the gyrus cinguli are concerned, experimental evidence is scant, owing to the inaccessibility of this region. I [29] have noted (pages 50 and 72) that in the two sexes the precuneus shows a greater difference in size than any other portion of the cortex, being more highly developed in the male, and it was suggested that representation of the sex organs may be localized there. This difference between the sexes has been confirmed by Mettler [30] (page 319) in the brain of the monkey. Sensations related to sex matters possess a high degree of emotional coloring.

More important evidence is derived from tumor of the corpus callosum which involves the surrounding cortex. Bristowe [31] described

26. Clark, W. E. L., and Boggon, R. H.: On the Connections of the Anterior Nucleus of the Thalamus, J. Anat. **67**:215-226, 1933.

27. Waller, W. H.: Topographical Relations of Cortical Lesions to the Thalamic Nuclei in the Albino Rat, J. Comp. Neurol. **60**:237-269, 1934.

28. Walker, E. A.: An Experimental Study of the Thalamo-Cortical Projection of the Macaque Monkey, J. Comp. Neurol. **64**:1-40, 1936.

29. Papez, J. W.: The Brain of Helen H. Gardener (Alice Chenoweth Day), Am. J. Phys. Antropol. **11**:29-79, 1927.

30. Mettler, F. A.: Brain of Pithecus Rhesus (M. Rhesus), Am. J. Phys. Anthropol. **17**:309-331, 1933.

31. Bristowe, J. S.: Cases of Tumor of the Corpus Callosum, Brain **7**:315-333, 1885.

the symptoms of slowly increasing paralysis, impairment of intelligence, progressive drowsiness, profound stupor, coma and death in cases of callosal tumor. Gowers [32] (page 712) expressed the opinion that the symptoms of tumor of the corpus callosum are due to pressure on or extension into the cerebral hemispheres. Ironside and Guttmacher [33] illustrated a number of such tumors, which clearly involved the gyrus cinguli of both sides. They stated:

> The mental changes which are so commonly present are often the first symptoms. Apathy, drowsiness and defect of memory are met with more commonly than in growths elsewhere, and occur with such regularity in the corpus callosum syndrome as to be characteristic.

Many similar cases can be found in the literature. In a recent paper, Voris and Adson [34] described the various symptoms and mental changes in thirty-eight cases. They listed the prominent mental changes as: loss of memory, indifference to environment, change in personality or character, drowsiness, stuporous or comatose state and disorientation in time and place. Less important are Witzelsucht, euphoria, puerility, delirium and states of depression. Armitage and Meagher [35] listed as first among the mental symptoms loss of spontaneity in emotion, thought and activity. Ligation or occlusion of the left anterior cerebral arteries produces marked reduction of conscious processes. Dandy [36] removed the various lobes of the hemispheres and ligated the left anterior cerebral artery and noted the effect on consciousness. He localized the seat of consciousness along the mesial aspect of the left hemisphere and near the corpus callosum. He, in agreement with others, recognized that steadily increasing pressure on the brain stem will produce drowsiness and eventually unconsciousness and postulated conduction tracts between the lower parts of the brain stem and the cortex which are responsible for conscious processes.

Occlusion of the anterior cerebral artery or its branches does not often destroy the gyrus cinguli, and even then rarely bilaterally. Critchley [37] described a case (case 2) in which there was softening of the left

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32. Gowers, W. R.: A Manual of Diseases of the Nervous System, Philadelphia, P. Blakiston's Son & Co., 1888.

33. Ironside, R., and Guttmacher, M.: The Corpus Callosum and Its Tumors, Brain **52**:442-483, 1929.

34. Voris, H. C., and Adson, A. W.: Tumors of the Corpus Callosum: Pathologic and Clinical Study, Arch. Neurol. & Psychiat. **34**:965-972 (Nov.) 1935.

35. Armitage, G., and Meagher, R.: Gliomas of the Corpus Callosum, Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:454-488, 1933; abstr., Arch. Neurol. & Psychiat. **33**:1112 (May) 1935.

36. Dandy, W. E.: Seat of Consciousness, in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1931, vol. 12, p. 57.

37. Critchley, M.: The Anterior Cerebral Artery, and Its Syndromes, Brain **53**:120-165, 1930.

paracentral lobule and the gyrus cinguli. The initial symptoms were fright, followed by a hysterical fit, semicoma and unconsciousness. As this condition improved, the patient was emotional, irritable and depressed, till the time of her death.

Cogent argument can be drawn from such evidence in support of the view that the gyrus cinguli is the seat of dynamic vigilance by which environmental experiences are endowed with an emotional consciousness. It seems likely that if ever the purely callosal symptoms are separated from the other cortical symptoms, the loss of emotive dynamics will be attributed to the compression or damage of the gyri cinguli, the strong associations of which with the hippocampal formations have already been outlined. There seems to be ample justification for the ancient view of La Peyronie, professor of surgery at Montpellier, who on the basis of such clinical experience expressed the belief that the region of the corpus callosum is the "seat of the soul" (quoted from Critchley [37]).

THE MAMILLARY BODY

In reptiles the hippocampus is connected with the hypothalamus in a diffuse way through the rudimentary fornix. The mamillary body is still undifferentiated, but this general cellular region is connected with the anterior thalamic nuclei, the connection of which in turn is chiefly with the corpus striatum. One can infer that hippocampal activity, however aroused, influences the hypothalamus in a diffuse way and through the striatal connections regulates attitudes of emotional expression. I [38] have suggested (page 469) that in reptiles the anterior nuclei may have an incipient connection with the frontal, parahippocampal cortex, which would correspond in part to the gyrus cinguli of mammals.

In mammals the mamillary bodies as well as the gyri cinguli, with which they connect, are always well developed. Many descriptions of these nuclear masses exist. For the present purpose it may be assumed that the description given by Aronson and me [39] (page 10) for the monkey is widely applicable to other forms. A good histologic description is that of Ramón y Cajal.[9] Cytologic details and connections were given. In brief, the mamillary body consists of a number of nuclei. The medial mamillary nucleus is the largest. The fornix ends chiefly in its lateral part. The larger medial part emits the mamillothalamic tract, or the fasciculus of Vicq d'Azyr. The lateral mamillary nucleus is a triangular mass of large cells in direct connection with the mamillary

38. Papez, J. W.: Thalamus of Turtles and Thalamic Evolution, J. Comp. Neurol. **61**:433-475, 1935.

39. Papez, J. W., and Aronson, L. R.: Thalamic Nuclei of Pithecus (Macacus) Rhesus: I. Ventral Thalamus, Arch. Neurol. & Psychiat. **32**:1-26 (July) 1934.

peduncle, which, according to the author, is an afferent bundle. This nucleus emits fibers which join the mamillothalamic tract. On the lateral side there also occurs the intercalate nucleus. Dorsally, in the supramamillary decussation is the supramamillary nucleus. A thin layer of cells separates the medial mamillary nuclei of the two sides and extends into the fibrous capsule of the bodies.

There are at least three direct afferent paths to the mamillary body. In general the capsule receives fibers from the tuber cinereum and the medial bundle of the forebrain, which Ramón y Cajal designated as the *faisceau de la capsule du corps mamillaire interne.*

The major part of the fornix ends by terminal collaterals in the medial nucleus of the mamillary body. A part of the fornix in some mammals (e. g., the guinea-pig) decussates dorsal to the mamillary body, and a part of this crossed bundle is continued to the interpeduncular region. This caudal bundle is conspicuous in some reptiles (e. g., Anolis carolinensis).

The mamillary peduncle may be interpreted as an ascending bundle coming from the region of the medial lemniscus and the medial border of the substantia nigra. In this region I [40] have identified (page 98) a special nucleus which I have designated as the nucleus of the mamillary peduncle. It appears likely from the observations of Edinger and Wallenberg [41] that the medial lemniscus is related to this structure. One can infer that proprioceptive impulses are thus brought into the mamillary body. However, the confusing views on the origin and polarity of the mamillary peduncle reviewed by Ramón y Cajal,[9] Huber and Crosby [42] and others must for the present remain an obstacle to any final interpretation of this fiber tract.

From these connections it is evident that the mamillary body receives impulses from the hippocampus, the tuber cinereum and other sources.

The mamillothalamic tract, or fasciculus of Vicq d'Azyr,[43] is the well known efferent tract from the mamillary nuclei to the anterior and anterodorsal nuclei of the thalamus. Its smaller part arises from the lateral mamillary nucleus. Near its origin the fasciculus bifurcates, giving off a smaller descending mamillotegmental tract, which, according to most authors, terminates in relation to the tegmental nuclei of Gudden. Stimulation along its course gives striking pressor effects, that

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40. Papez, J. W.: Thalamic Nuclei of the Nine-Banded Armadillo, J. Comp. Neurol. **56**:49-103, 1932.

41. Edinger, L., and Wallenberg, A.: Untersuchungen über den Fornix und das Corpus mammillare, Arch. f. Psychiat. **35**:1, 1902.

42. Huber, G. C., and Crosby, E. C.: Somatic and Visceral Connections of the Diencephalon, Arch. Neurol. & Psychiat. **22**:187-229 (Aug.) 1929.

43. Vicq d'Azyr, F.: Traité d'anatomie et de physiologie, Paris, F.-A. Didot l'Aîné, 1776.

is, rise of blood pressure. As the main mamillothalamic tract ascends, it gives off these collaterals in the region of the nucleus campi Foreli of the Vogts.[44]

It is thus seen that the mamillary body can mass and relay the impulses it receives to the anterior thalamic nuclei and, to a lesser extent, to the deep tegmental nuclei. Kernohan, Learmonth and Doyle[45] (case 4) reported a case of tumor in the third ventricle which destroyed the tuber cinereum and the corpora mamillaria. The patient was drowsy most of the time; she had diabetes insipidus, and during occasional attacks of weakness she perspired profusely.

The recent work of Ranson,[4] with the aid of Ingram, showed not only that damage in and around the mamillary bodies causes drowsiness and somnolence in monkeys but that during this period the animals are emotionally inactive. They lost their wildness and even after recovery from somnolence were tame and tractable. When it is remembered that the sensory pathways to the cortex were not interrupted, the importance of the mamillothalamic cortical pathway in insomnia and emotional excitement can be appreciated.

THE ANTERIOR NUCLEI OF THE THALAMUS

How the anterior and the anterodorsal nuclei receive the fasciculus of Vicq d'Azyr and how they connect with the gyrus cinguli, on the one hand, and the head of the corpus striatum, on the other, have already been stated.

Clinical data on the anterior thalamic nuclei are meager, but emotional disturbances, such as spontaneous laughing and crying, from thalamic lesions are well authenticated. Perhaps the most vivid case of compression in this region was described by Penfield[46] as one of diencephalic autonomic epilepsy produced by a tumor situated at the interventricular foramen, between the anterior thalamic nuclei and back of the column of the fornix.

> The patient lay most of the time in obvious pain. At intervals she had an attack in which the same phenomena appeared regularly. The attack was explosive and was confined to the structures controlled by the vegetative nervous system. Prodromal symptoms were restlessness and a request for ice in the mouth, followed by sudden vasodilatation of the area of the skin supplied by the cervical sympathetic nerves. There were sudden rise of blood pressure, lacrimation, salivation, dilatation of the pupils, protrusion of the eyes, increase in pulse rate, retardation

44. Vogt, O., and Vogt, C.: Zur Kenntnis der pathologischen Veränderungen des Striatum und des Pallidum, Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturw. Cl. (Abt. B) **14**:1-56, 1919.

45. Kernohan, J. W.; Learmonth, J. R., and Doyle, J. B.: Neuroblastomas and Gangliocytomas of the Central Nervous System, Brain **55**:287-310 (Sept.) 1932.

46. Penfield, W.: Diencephalic Autonomic Epilepsy: The Vegetative Nervous System, A. Research Nerv. & Ment. Dis., Proc. **10**:645-663, 1930.

of the respiratory rate, excitability of the pilomotor reflex and loss of consciousness. The attack lasted ten minutes or more. As the symptoms faded, transient hiccup, shivering and respiration of the Cheyne-Stokes type occurred, followed by drowsiness and a tendency to sleep.

Cases of tumors destroying these thalamic nuclei have been recorded. Mott and Barratt [47] (case 1) described a case in which the tumor involved the anterior thalamic nuclei. Among other symptoms the patient exhibited drowsiness, sometimes falling asleep while taking food. Weisenburg [48] discussed the question whether lesions of the third ventricle cause mental symptoms, such as apathetic, dull mentality, drowsiness and somnolence. Fulton and Bailey [49] (case 3) reported a case of hypersomnia due to a cystic tumor of the anterior part of the third ventricle. Hart remarked that "emotional negativism and fatuous serenity are states of mind described by numerous authors." There is little doubt that tumor of this region produces loss of emotive dynamics when it involves the mamillary body, the fasciculus of Vicq d'Azyr or the anterior thalamic nuclei. On the other hand, lesions of the tuber and the pars optica produce diabetes insipidus, Fröhlich's syndrome and other disturbances of the autonomic nervous system, with less marked emotional changes.

THE SUPRA-OPTIC DECUSSATIONS AND THE PARS VENTRALIS THALAMI

The commissures of Meynert, Ganser and Gudden are well entrenched in neurologic literature, though their functional significance is veiled in obscurity. Concerning the origin and ending of these supra-optic decussations the evidence is still conflicting and weighted with the opinions of older authors, e. g., Bechterew,[14] Dejerine,[11] Edinger [22] and others.

By older authors the origin of Meynert's commissure, as well as its termination, was given as pallidal. So closely are the pallidum and its ansa lenticularis applied to the optic tract that they are superimposed on Meynert's commissure, and it looks as if the commissure arose from the pallidum. Hence the classic view.

Somewhat contrary to this view it has been shown that in some of the lower mammals [40] (page 94) and in reptiles [38] (page 452) what appears to be the equivalent of Meynert's commissure arises from the

47. Mott, F. W., and Barratt, J. O. W.: Three Cases of Tumors of the Third Ventricle, Arch. Neurol. Path. Lab. London County Asyl. Claybury **1**:417-439, 1900.

48. Weisenburg, T. H.: Third Ventricle Tumors, Brain **33**:236-260, 1910.

49. Fulton, J. F., and Bailey, P.: Tumors in the Region of the third Ventricle: Their Diagnosis and Relation to Pathologic Sleep, J. Nerv. & Ment. Dis. **69**:1-25, 1929.

pars ventralis of the lateral geniculate body and the pregeniculate nucleus. Passing along the optic tract, it appears to end in the pars ventromedialis of the supra-optic nucleus. In part it decussates, to end in the hypothalamus of the other side. Accordingly, it represents an afferent connection between the primitive optic centers of the ventral thalamus and the hypothalamus. This point of view has already been indicated by Vonderahe.[50]

In the same papers it has also been intimated that the dorsal supra-optic decussation corresponds to the fibrae ansulatae, Ganser's commissure or the anterior hypothalamic commissure in the anterior part of the tuber cinereum. In reptiles these fibers arise from the nucleus of the dorsal supra-optic decussation (Huber and Crosby [42] and others), situated in the course of the lateral bundle of the forebrain. My own observations on the brains of various mammals (e. g., dog, monkey and man) lead me to believe that the fibers issue in part from a fiber mass situated lateral to the pillar of the fornix, in area P_3 of Winkler,[51] which is interpolated in the course of the oral portion of the pallido-rubro-olivary and other fibers of ansa lenticularis. In Carnivora the pallidohypothalamic fibers come from the entopeduncular nucleus, and in the monkey and in man, from a comparable region, namely, the medial nucleus or segment, of the globus pallidus (Grünthal [52]). I have verified experimentally in the cat that the other coarse fibers of the anterior hypothalamic commissure come from the region of the interstitial nucleus of the midbrain, as described by others.[42]

Concerning Gudden's commissure, it is generally admitted that its origin is in the inferior colliculus, the posterior portion of the tectum (Huber and Crosby [42]), and in most lower vertebrates also in the nucleus isthmi or parabigeminal body. En route, as it joins the optic tract, it also receives fibers from the pars ventralis of the medial geniculate body (Papez [53] and others). Decussating with the optic tract, it probably ends in the anterior portion of the tuber cinereum, and according to the classic view, many of its fibers may reach the medial geniculate body of the opposite side. Thus, it represents an afferent connection between the primitive acoustic and static centers and the hypothalamus.

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50. Vonderahe, A. R.: The Representation of Visceral Function in the Brain, Ohio State M. J. **31**:104-109, 1935.

51. Winkler, C.: Manuel de neurologie. Le corps strié et le diëncéphale, Haarlem, de Erven F. Bohn, 1933, vol. 1, pt. 5, p. 34.

52. Grünthal, E.: Vergleichend anatomische Untersuchungen über den Zellbau des Globus pallidus und Nucleus basalis der Säuger und des Menschen, J. f. Psychol. u. Neurol. **44**:403-428, 1932.

53. Papez, J. W.: Evolution of the Medial Geniculate Body, J. Comp. Neurol. **64**:41-61, 1936.

As has already been said, it is possible that the mamillary peduncle represents a similar primitive connection of the medial lemniscus, the proprioceptive pathway and of the substantia nigra, to the mamillary body.

Concerning the olfactory centers and the amygdala, the case is simple. The medial bundle of the forebrain connects the septal region and the olfactory tubercle with the whole extent of the lateral hypothalamic nuclei. The stria terminalis connects the amygdala, the function of which is unknown, with the pars optica hypothalami (Johnston,[54] Krieg [55] and others).

The question remains how the reticular nucleus and the remaining receptive portions of the pars ventralis thalami are connected with other regions of the brain. Some good evidence was derived from the myelinization studies of Bechterew,[14] from the Marchi experiments of Wallenberg [56] and from the observations of others that ascending spinothalamic and bulbothalamic tracts end in part in these nuclei. The reticular nucleus is generally credited with sending fibers broadcast to the cerebral cortex. Connections with the pallidum and the hypothalamus are possible. What function it mediates is unknown, though its primitive nature is certain. In this regard the thalamic pain syndrome of Dejerine and Roussy [57] deserves reconsideration, as do the visceral and gustatory functions of the amygdala.

In recent papers of Krieg,[55] Clark,[58] Papez and Aronson [39] and Walker, [28] the connections in the medial walls of the third ventricle have been emphasized. There is no question of the existence of such periventricular fibers, as they can be clearly seen in the brains of reptiles and of most mammals. Especially important are the connections between the medial nucleus and centrum medianum and the hypothalamus. The view of Nathan [59] on the localization of emotions and personality in the region of the third ventricle appears to have considerable anatomic support. He reviewed the historical development of this idea from

54. Johnston, J. B.: Cell Masses in the Forebrain of the Turtle, Cistudo Carolina, J. Comp. Neurol. **25**:393-468, 1915.

55. Krieg, W. J. S.: The Hypothalamus of the Albino Rat, J. Comp. Neurol. **55**:19-89, 1932.

56. Wallenberg, A.: Sekundäre sensible Bahnen im Gehirnstamme des Kaninchens, ihre gegenseitige Lage und ihre Bedeutung für den Aufbau des Thalamus, Anat. Anz. **24**:142 and 357, 1904.

57. Dejerine, J., and Roussy, G.: Le syndrôme thalamique, Rev. neurol. **14**: 521-532, 1906.

58. Clark, W. E. L.: Structure and Connections of the Thalamus, Brain **55**: 406-470, 1932.

59. Nathan, M.: Le troisième ventricule constitue-t-il un cerveau affectif? Presse méd. **39**:857-858 (June 10) 1931.

Haškovec (1910, 1925 and 1929) to Camus (1921, 1924), Roussy and Lhermitte (1924), Rosenfeld (1925) and Küppers (1929).

The left basal region was suspected by Alford.[60] His observations showed that emotion and consciousness are not located primarily in the lateral cortex of the cerebral hemispheres and that they are more disturbed by basal lesions of the left hemisphere.

SUMMARY

Is emotion a magic product, or is it a physiologic process which depends on an anatomic mechanism? An attempt has been made to point out various anatomic structures and correlated physiologic symptoms which, taken as a whole, deal with the various phases of emotional dynamics, consciousness and related functions. It is proposed that the hypothalamus, the anterior thalamic nuclei, the gyrus cinguli, the hippocampus and their interconnections constitute a harmonious mechanism which may elaborate the functions of central emotion, as well as participate in emotional expression. This is an attempt to allocate specific organic units to a larger organization dealing with a complex regulatory process. The evidence presented is mostly concordant and suggestive of such a mechanism as a unit within the larger architectural mosaic of the brain.

Negative and contradictory evidence has not been presented. The structures described here are usually represented as dealing with some phase of the olfactory function. There is no clinical or other evidence to support this view. The new interpretation which I propose can be supported by much more data at present available in the literature, but it is evident that any such doctrine will have to stand the test of experimental and clinical experience if it is to be useful in science. Emotion is such an important function that its mechanism, whatever it is, should be placed on a structural basis.

The organization presented here meets adequately the physiologic requirements proposed by Cannon and Bard in respect to the theory of emotion based on diencephalic-cortical processes. It is also in agreement with the observations of Dandy[36] that the seat of consciousness is located somewhere near the midline, between the limits set by the corpus callosum and the basal structures of the brain.

60. Alford, L. B.: Localization of Consciousness and Emotion, Am. J. Psychiat. **12**:789-799, 1933.

MODE OF ONSET OF EPILEPSY

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Experience with a fairly large number of epileptic patients shows striking differences among them. There are vital differences not only as to etiology (Cobb [1]) but also as to the manner in which the illness sets in, its evolution and its clinical manifestations. In fully developed epilepsy the attacks usually show an assortment of features, including psychic, visceral and motor symptoms.

In this study we directed attention to the mode of onset and noted that the illness commonly began in one of two ways. In some patients epilepsy set in abruptly; a person previously well fell to the ground in a sudden, violent convulsion. In other patients the disease set in gradually, beginning with slight, peculiar sensations, which recurred with added features until, in the course of months or years, true epileptic characteristics became evident. The first type may be considered as abrupt or violent; the second may be designated as mild, gradual or insidious. In recent literature the second type has been referred to as a "forerunner of epilepsy" (Levy and Patrick [2]) and as "larvaceous epilepsy" (Albert-Weil [3]).

Does the mode of onset have any significance for the course of the disease? Consideration of this problem is our purpose in this paper.

MATERIAL AND METHOD

The group studied in this series were from an outpatient clinic for epilepsy. In the main they had chronic epilepsy; all, at one time or another, had had convulsive seizures. From this large group, 160 of the better studied cases were

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From the Neuropsychiatric Dispensary, the Lakeside Hospital and the Western Reserve University School of Medicine.

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1. Cobb, S.: Causes of Epilepsy, Arch. Neurol. & Psychiat. **27**:1245 (May) 1932.

2. Levy, D. M., and Patrick, H. T.: Recurrent "Attacks" Other Than Migraine and Infantile Convulsions Preceding "True" Epilepsy, Arch. Neurol. & Psychiat. **20**:443 (Sept.) 1928.

3. Albert-Weil, J.: Epilepsie larvée, Rev. gén. de clin. et de thérap. **46**:805 (Dec. 3) 1932.

selected. In practically every instance there had been an extensive history, complete neurologic examination and routine roentgenographic and laboratory procedures. In some cases encephalography, sugar tolerance tests and other investigations were undertaken. Intelligence tests were made by a psychologist, Mrs. M. Barnes, the average intelligence quotient (Binet-Simon) for the entire group being 74 (Fetterman and Barnes [4]). Most of the patients have been followed in the clinic for a long time.

Of the 160 patients 102 were considered as belonging to the group with so-called idiopathic, or cryptogenic, epilepsy, 51 to the group with the organic type and 7 to the group with the psychogenic type (table 1). It must be admitted, however, that rigid distinctions as to etiologic type are not practical or tenable.

TABLE 1.—*Classification of All Cases in This Study as to Etiologic Type*

Type	Number Cases	Total
Idiopathic		102
Organic		51
Developmental and congenital	7	
Traumatic	11	
Childhood (before 14)	6	
Adult	5	
Postencephalitic	15	
Childhood (before 14)	14	
Adult	1	
Tumor of brain	11	
Syphilitic	1	
Toxic (alcoholic)	6	
Psychogenic		7
Total		160

TABLE 2.—*Comparison of "Violent" and "Mild" Modes of Onset in the Entire Series, Subdivided According to the Three Main Etiologic Groups*

Etiologic Type	Violent Onset (Grand Mal Convulsion as Initial Episode), Percentage of Cases	Mild Onset (Petit Mal Seizure or Mild Equivalents as Initial Episode), Percentage of Cases
Idiopathic	79.4	20.6
Organic	76.5	23.5
Psychogenic	71.7	28.3

Thus, it was believed that the condition should be classified as traumatic only when there was definite evidence of significant cerebral trauma as evaluated by Kennedy.[5] A diagnosis of psychogenic epilepsy was made with reluctance. Indeed, of a group of patients whose condition was diagnosed at one time as hystero-epilepsy 2 later presented evidence of organic disease—1 of these a tumor of the brain.

It was our aim to determine what significance the mode of onset had for the various qualities of the disease. We therefore tabulated our material and correlated the mode of onset with the various outstanding features, such as etiology,

4. Fetterman, J., and Barnes, M.: Serial Studies of Intelligence of Patients with Epilepsy, Arch. Neurol. & Psychiat. **32**:797 (Oct.) 1934.

5. Kennedy, F.: Head Injuries: Effects and Their Appraisal; Evaluation of Evidence, Arch. Neurol. & Psychiat. **27**:811 (April) 1932.

age at onset, intelligence quotient, family history, eventual severity and response to therapy. The findings are presented in tabulated form, and a discussion follows.

ANALYSIS OF TABULATIONS

Table 2 shows the relative frequencies in the various larger etiologic groups of (1) the violent and (2) the mild modes of onset. In this differentiation, with which we are concerned in this paper, the term "violent" is used to include all cases in which the initial episode was a grand mal convulsion, either jacksonian or generalized. The designation "mild" refers to the forms of onset which were momentary, minor disturbances in the motor, sensory or psychic functions. These include "blank spells," "stares," giddy and dizzy feelings, uncomfortable visceral sensations, etc. These experiences proved to be petit mal attacks or were incorporated into the aura of later grand mal attacks. It is probable that the incidence of epilepsy initiated by mild episodes is even larger than our figures indicate,

TABLE 3.—*Correlation of Mode of Onset with Age at Onset*

Age Group	Violent Onset (Grand Mal), Percentage of Cases in This Age Group	Mild Onset (Petit Mal or Mild Equivalent), Percentage of Cases in This Age Group	Total Percentage of All Cases in This Age Group
A. 102 Cases of Idiopathic Epilepsy			
0-10 years	26.0	47.8	30.4
11-20 years	51.8	38.1	49.0
21 years and older	22.2	14.1	20.6
Total	100 (81 cases)	100 (21 cases)	100 (102 cases)
B. 15 Cases of Postencephalitic Epilepsy			
0-10 years	33.3	66.7	40.0
11-20 years	58.4	33.3	53.3
21 years and older	8.3	0.0	6.7
Total	100 (12 cases)	100 (3 cases)	100 (15 cases)

since doubtless in many cases these minor initial episodes were disregarded by the patient and informant and hence the onset was dated only from the first grand mal seizure.

The relative frequencies of the two modes of initial manifestation were strikingly uniform for the three groups—idiopathic, organic and psychogenic. In each group the disease in from about one fourth to one fifth of all cases began as episodes so mild that only later did the true epileptic nature become evident. This fact emphasizes the necessity of being on the alert for these mild episodes as possible early manifestations of epilepsy. On the other hand, as will become evident in the later discussion of our findings, by no means all similar episodes, or even convulsive seizures, are epileptic.

Table 3 (*A* and *B*) shows the trend of distribution as to age at onset in cases in which the condition began with violent or mild episodes, respectively. There is necessarily such wide difference as to the age at onset in various etiologic types (e. g., birth trauma, alcoholism or tumor of the brain) that figures can be compared only within individual groups. To table 3 *A*, which gives figures for the group with idiopathic epilepsy, we appended for comparison table 3 *B*, showing those for the group with postencephalitic type, which, though not large, is the largest of the

remaining groups. There may be seen in both groups a definite tendency for patients with onset of mild petit mal to be in lower age groups than those with onset of violent grand mal (e. g., in one half of all patients with idiopathic epilepsy with mild onset the seizures began in the first decade of life, as compared with only one fourth of those with violent onset). In the group with postencephalitic epilepsy, the encephalitis occurred, with one exception, in the first decade of life, and, with a few exceptions, in the first two years of life.

Table 4 *A* shows the incidence of a positive family history of epilepsy or other neuropathic taint in all cases. In our series we included in the positive family history persons with a neuropathic taint in the direct line in siblings or in a collateral line once removed. Our figures agree in the main with the observations of others (Oppenheim,[6] Muskens[7] and Snell[8]); 53 per cent had a family history of neuropathic taint, and 24.5 per cent a history of one or more epileptic persons in the family. We note that the percentage is somewhat lower for the group with organic epilepsy than for that with the idiopathic type. However, the fact that it reaches

TABLE 4.—*Correlation of Family History of Neuropathic Taint with Incidence and Mode of Onset of Epilepsy*

Etiologic Type or Mode of Onset	Number of Cases	Family History of Epilepsy, Percentage of Cases	Family History of Other Types of Neuropathologic or Psychopathologic Condition, Percentage of Cases	Total Percentage of Cases in Which There Was Family History of Neuropathic Taint
A. Incidence of Positive Family History in Direct or a Collateral Line Once Removed (160 Cases)				
Idiopathic	102	24.5	28.4	52.9
Organic	51	19.6	13.6	33.2
Psychogenic	7	14.1	28.2	42.3
B. Correlation of Positive Family History with the Mode of Onset (102 Cases of Idiopathic Epilepsy)				
Violent (grand mal)	81	27.2	27.2	54.4
Mild (petit mal or mild equivalent)	21	14.2	33.3	47.5

even that height in cases of the organic type may signify that a familial tendency is one of the determinants as to whether in the cases of organic insult convulsive seizures will be numbered among the symptoms.

Table 4 *B* shows the percentage of persons with a positive family history in relation to the mode of onset in idiopathic epilepsy (the largest individual group). There are no definite differences, although the percentage of familial epilepsy per se is lower in the group with mild onset (i. e., 14 per cent as compared with 27 per cent).

Table 5 shows the distribution of persons with epilepsy of violent and of mild onset as to the intelligence quotient. The standard Binet-Simon tests were given to 84 patients of the series, some of whom were tested several times. Here again,

6. Oppenheim, H.: Textbook of Nervous Diseases for Physicians and Students, Edinburgh, O. Schulze & Co., 1911.

7. Muskens, L. J. J.: Epilepsy: Comparative Pathogenesis, Symptoms, Treatment, New York, William Wood & Company, 1928.

8. Snell, O.: Die Belastungsverhältnisse bei der genuinen Epilepsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **70**:1, 1921.

there are no definite differences in the intelligence quotients of the two groups. If there is any correlation at all, the tendency is for patients with mild onset to have a little higher intelligence quotient than those with violent onset. There is a slightly greater percentage of instances of mild onset among persons with intelligence quotients between 90 and 110. Those with the lowest intelligence ratings (quotients under 50) all showed a violent onset. (To be sure, persons with extremely low intelligence may be less observant or less capable of describing or reporting the finer shades of feeling and sensation and so may tend to date the onset only from the first violent seizure. Thus, even this slight difference may be more apparent than real.)

TABLE 5.—*Correlation of Intelligence Quotient with the Mode of Onset in 84 Cases of Idiopathic Epilepsy*

Intelligence Quotient	Violent Onset (Grand Mal), Percentage of Cases in This Group	Mild Onset (Petit Mal or Mild Equivalent), Percentage of Cases in This Group	Total Percentage of All Cases in This Group
90-110	17.0	26.4	19.0
70- 90	41.5	36.8	40.5
50- 70	35.4	36.8	35.7
50 and lower	6.1	0.0	4.8
Total	100 (65 cases)	100 (19 cases)	100 (84 cases)

TABLE 6.—*Correlation of Eventual Severity with the Mode of Onset in 102 Cases of Idiopathic Epilepsy*

Grade of Severity (Graded by Summation of Severity of Individual Seizures and Frequency)	Violent Onset (Grand Mal), Percentage of Cases in This Group	Mild Onset (Petit Mal or Mild Equivalent), Percentage of Cases in This Group	Total Percentage of All Cases in This Group
Very mild	7.4	23.8	10.8
Moderately mild	30.9	23.8	29.4
Moderately severe	37.0	33.3	36.3
Very severe	24.7	19.1	23.5
Total	100 (81 cases)	100 (21 cases)	100 (102 cases)

Of interest to compare with these figures is the fact that our particular group of patients showed no definite relationships either between the intelligence quotient and age at onset or between the intelligence quotient and family history. These findings are at variance with those of Paskind,[9] who found a history of high familial incidence to be correlated with early onset, a low intelligence quotient and mental deterioration.

Table 6 shows the degree of eventual severity in 102 cases of idiopathic epilepsy. There are demonstrated no significant correlations between the two groups as to their eventual state. For very mild epilepsy, to be sure, the percentage of

9. Paskind, H. A.: Extramural Patients with Epilepsy, with Special Reference to Frequent Absence of Deterioration, Arch. Neurol. & Psychiat. **28**:370 (Aug.) 1932.

cases of mild onset is higher (about 25 per cent); that is, in about one fourth of the cases of mild onset the condition remained mild, perhaps with only one or two grand mal seizures in the entire course, as long as it was followed (up to fifteen years). However, this percentage would have been even higher if the cases had been included in which petit mal seizures persisted throughout, a group which was purposely excluded from our study. If, then, the cases of a somewhat borderline type are not included, there are no significant relationships between the mode of onset and the eventual severity.

As a corollary to the foregoing findings, there was no definite correlation between the mode of onset and the response to therapy in 58 patients with idiopathic epilepsy who were treated with phenobarbital, ipral, dehydration and acidosis, and followed over sufficient periods.

Table 7 shows the latent interval between the time of occurrence of a known cerebral lesion and the age at onset of both violent and mild seizures. In studying

TABLE 7.—*Latent Interval Between Time of Occurrence of Injury to the Brain and the Onset of Symptoms of Mild or Severe Convulsive Nature in 32 Cases of Organic Epilepsy in Which the Nature and Time of Occurrence of Cause Was Known*

Etiologic Type, Number of Cases	Total Number of Cases of the Etiologic Group		Violent Onset (Grand Mal), Median Latent Interval	Mild Onset (Petit Mal or Mild Equivalent), Median Latent Interval
	Range of Latent Interval	Median Latent Interval		
Developmental and congenital (7).....	Birth to 13 years	1 year	1 year	21 months
Traumatic				
Birth and childhood (5).....	1 month to 8 years	1 month	1 month	.....
Adult (5).....	1 month to 3 years	2 years	2 years	2 years
Postencephalitic (15).....	Immediate to 16 years	8 years	9 years	1 year
Total (32).....	Immediate to 16 years	18 months		

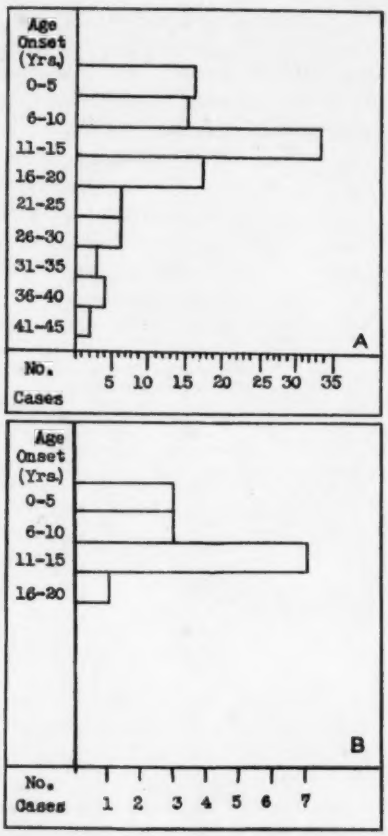
this phase of the problem, 32 persons with organic epilepsy were used for whom the date of occurrence of the cerebral lesion was accurately known.

As may be seen in the table, there was considerable variation in the length of this interval for the different etiologic groups. For example, in the group with the developmental and congenital type the median latent interval was one year; in patients who had suffered trauma in infancy or childhood, one month, and in adults who had trauma, two years; for children who had had encephalitis there was a longer period, which averaged eight years from the time of the encephalitis to the onset of epilepsy. These figures represent the median latent interval, although the time which elapsed in individual cases ranged from immediate onset of epilepsy to an interval of sixteen years. There was no close correlation between the length of this latent interval and the mode of onset. However, the number of cases in each individual group is small, and therefore the significance of the figures should not be overrated. The meaning of this latent interval will be discussed later.

Chart *A* shows graphically the age at onset of symptoms of 102 persons with idiopathic epilepsy. This graph shows the concentration to be at about puberty,

which is characteristic for extramural patients as contrasted with institutionalized patients (Lennox and Cobb [10]).

Chart *B* shows graphically the age at which the first symptoms (violent or mild) appeared in 14 cases of postencephalitic epileptic seizures. In all but 2 cases, in which the illness was at the age of 6 and 7 years, respectively, the encephalitis occurred in the age group of less than 5 years. Here again one finds a similar concentration of onset about puberty.



Age of onset (*A*) in 102 cases of idiopathic epilepsy and (*B*) in 14 cases of postencephalitic epilepsy occurring in infancy and in childhood.

COMMENT

As may be seen in the preceding tables, the onset occurred abruptly in from 75 to 80 per cent of the cases and mildly in the remainder. Except for the alcoholic group, to be discussed later, there was remarkable uniformity in this ratio for all etiologic types, the organic and the

10. Lennox, William G., and Cobb, Stanley: The Non-Institutional Epileptic, A. Research Nerv. & Ment. Dis., Proc. **7**:358, 1931.

idiopathic group showing apparently the same percentages of violent and mild onsets.

The reason for this variation in the mode of onset is not entirely clear. It would appear that the normal central nervous system possesses immunity or resistance to epilepsy. This resistance may be broken down abruptly in some instances and gradually in others.

With reference to the age at onset: There was a slight tendency for the lighter modes to occur in young persons. Thus, in 48 per cent of cases in which the onset was insidious, the disease began in the first decade of life, as compared with only 26 per cent in which there was abrupt, violent onset.

Our small series of cases shows the significance of early attacks, either abrupt or mild, for the development of later chronic epilepsy. Several studies by neurologists have emphasized the possible seriousness of convulsive attacks in childhood. Thom [11] found that of 265 patients selected at random who had convulsions in childhood, 16 per cent were mentally deficient and 13 per cent continued to have epilepsy. Levy, in a discussion of Thom's paper, stated: "A child with infantile convulsions assumes five times the risk of the ordinary child in acquiring epilepsy." A similar serious interpretation was given by Heuyer and Dublineau.[12] They found that convulsions in childhood may be followed by epilepsy in approximately 30 per cent of cases. A less serious interpretation of infantile convulsions was given by Shanahan [13] and by Eckstein,[14] but attention may be called to the fact that not only convulsive seizures in childhood but the milder forms as well may have an equally important significance for later epilepsy, for both indicate either a cerebral lesion or a nervous system which is susceptible to attacks.

There was no important correlation between the mode of onset and the intelligence quotient of the patient. There was only the slightest tendency for milder forms of onset to occur in persons with higher intelligence. It has already been suggested that even this variation may well be erroneous.

With reference to the severity and course of the disease: It is evident that the mildness of the onset is not a measure of the eventual

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11. Thom, D. A.: Infantile Convulsions: Their Frequency and Importance, Am. J. Psychiat. **6**:613, 1927.

12. Heuyer, G., and Dublineau, J.: Convulsions de l'enfance dans leurs rapports avec l'épilepsie, Rev. neurol. **1**:1292, 1932.

13. Shanahan, W. T.: Convulsions in Infancy and Their Relationship, If Any, to Subsequent Epilepsy, Am. J. Psychiat. **7**:591, 1928.

14. Eckstein, A.: Ueber die Beziehungen der "kindlichen Epilepsie" bzw. genuinen Epilepsie zu den Krämpfen des Kindesalters, Klin. Wchnschr. **13**:1201 (Aug. 25) 1934.

severity of the epilepsy. Apparently, like percentages of mild forms of onset occurred in patients who had chronic severe epilepsy and in those who suffered only occasional or mild attacks. Regularly, persons who began with momentary "stares" or transient visceral sensations later experienced diminution in consciousness and, finally, complete loss of consciousness with all the convulsive features of epilepsy. In some instances, to be sure, there was a tendency for epilepsy with a mild onset to remain mild throughout the course of the disease.

In general, there was no important correlation between the severity of onset and the family history.

SPECIAL CONSIDERATIONS

Alcoholism and Epilepsy.—In 6 of the group of 160 patients, the condition was diagnosed as alcoholic epilepsy. This diagnosis was based on a history of alcoholism, a close time relationship between excessive drinking and the attacks and the absence of other significant history or of any objective evidence of other causes. For this group, the onset was uniform—the initial attack was a convulsive seizure. Though the cases were few, the fact that in 100 per cent the onset was abrupt may have meaning. What this meaning is we are not prepared to state. The explanation suggests itself that the influence of alcohol on the brain may be generalized rather than focal, as in trauma or tumor, or that alcoholic persons may resist attacks completely until the entire function is lost.

It is only fair to state that the observation of a violent mode of onset in 100 per cent of cases may not portray the true picture. It is possible that a person under the influence of alcohol may ignore slight disorders of the psychomotor system because consciousness is clouded or because the experiences may be looked on as a natural effect of the alcohol per se. We recently studied a patient with chronic alcoholism who had been troubled by recurrent attacks of exhaustion for which the designation "asthenolepsy" appeared appropriate. Whether this means that the spells of extreme weakness are the forerunners of later epilepsy time alone will tell.

Encephalitis.—During the course of this study we were impressed by the high incidence of epilepsy following infantile encephalitis, in contrast to its relative infrequency following adult lethargic encephalitis. This difference is not readily explained. It is possible that in the postinfectious encephalitis of childhood there is damage to a more sensitive area, such as the cortex, while in adult lethargic encephalitis the basal ganglia and the substantia nigra are involved. Also, the fact that puberty follows childhood encephalitis and precedes the adult forms may be of significance. The importance of puberty as an influence is illustrated by the high frequency of onset in the period between the

ages of 11 and 16 in our small number of cases, as well as in practically all the larger series (chart A).

PERIOD OF LATENCY (INCUBATION PERIOD)

In 32 cases of the organic group it was possible to estimate the interval between the occurrence of the lesion in the nervous system and the first attack. As table 7 shows, in the group with childhood encephalitis this interval ranged from immediate onset to sixteen years. For the group in which there was craniocerebral trauma the time which elapsed ranged from one month to eight years, our findings conforming in this regard to those in cases of injury to the head reported by other observers (Isserlin,[15] Stevenson [16] and Savitsky [17]). Cases are on record in which epilepsy did not appear until ten, fourteen, sixteen or even twenty years after the trauma to the head. The period between the injury of the brain and the onset of epilepsy may be looked on as a period of incubation, or as a latent interval.

It would seem to be a time during which the natural defenses of the brain against convulsions are being overcome. We were puzzled as to the significance of such a long interval. As yet we have no satisfactory explanation, though several theories suggest themselves. One might first think that it is a period during which scar tissue forms. Penfield and Foerster [18] have graphically described the development of posttraumatic scar as a cause of epilepsy. However, the interval in most patients with this injury is far in excess of that required for mere gliosis to take place. Were the influence of the scar all important, one might expect the epilepsy to appear within a few months.

In view of the fact that even in our small series of cases the interval ranged from one to sixteen years and in the light of reports of many cases of even later appearance of epilepsy, one must seek some other explanation. A theory suggests itself. There may be secondary factors, perhaps themselves incapable of producing attacks, which, when these are added to the original focus of injury, may together with it cause epilepsy.

Such secondary factors may be illustrated by the addition of alcoholic intoxication or emotional strain to a preexisting organic lesion.

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15. Isserlin, M.: Ueber die Bedeutung der Erfahrungen an Kriegshirngeschädigten, Nervenarzt **3**:569 (Oct. 15) 1930.

16. Stevenson, W. E.: Eilepsy and Gunshot Wounds of the Head, Brain **54**: 214, 1931.

17. Savitsky, N.: Epileptic Attacks Sixteen Years After Trauma of the Head. Arch. Neurol. & Psychiat. **26**:1087 (Nov.) 1931.

18. Foerster, O., and Penfield, W.: Structural Basis of Traumatic Epilepsy and Results of Radical Operation, Brain **53**:99, 1930.

For example, J. S. had sustained fracture of the skull at the age of 18 years. Seven years later, during a period of heavy drinking, the first convulsion appeared. Apparently the gliosis had taken place in the first few months, producing a sensitive area, which was dormant until alcohol induced the attack. In the case of M. M., the initial attack appeared during a sleepless night with anxiety and intense emotional strain. The condition was looked on as hystero-epilepsy, and only later did the true cause, a tumor of the brain, become evident. Apparently in this case, emotional stress was the factor which brought out the dormant cause.

As we have already indicated, the influence of puberty in this connection is important. In several cases of infantile encephalitis the first epileptic attack did not occur until the age of 12 or 14 years. Indeed, the length of the latent period was such as to make the first convulsion appear in adolescence in 50 per cent of the cases. Though the organic lesion in the brain was present early in every case, it remained latent as a cause of epilepsy until puberty, the general curve for incidence based on age paralleling that for noninstitutionalized patients with idiopathic epilepsy. It would seem as though a certain psychochemical constellation of puberty may break down the defenses against epilepsy.

The nature of this secondary factor is not always obvious. In the younger groups, emotional and puberal factors are significant. In the adult group, trauma, alcoholism, arteriosclerosis and emotional stress may serve as the "synergistic" factors.

Two deductions of practical significance may be made from this observation: 1. Medicolegal: As epilepsy may not appear until several years after craniocerebral trauma, should not settlements in such cases be postponed for a period or the probable factor of attacks be taken into consideration in the settlement? (We are making a more extended study of the relation of trauma to epilepsy.) 2. Therapeutic: From the standpoint of preventive treatment, would it not be advisable in every case of encephalitis or of trauma in childhood to prescribe in advance of attacks such sedatives or other kinds of medication as are thought to be useful, in the hope that future attacks may be prevented? For example, phenobarbital is considered valuable in active treatment for epilepsy and is apparently harmless for use over a long period. May it not be useful in a preventive way?

SUMMARY AND CONCLUSIONS

1. We have reviewed the histories of 160 patients suffering from chronic convulsive disorders, with particular reference to the mode of onset.

2. Our results indicate that in from 75 to 80 per cent of patients the initial symptom is a convulsive seizure, and in from 20 to 25 per cent the first manifestation is a mild, light disturbance, resembling

a petit mal attack or the later aura. This proportion was practically the same in the group with organic and with idiopathic epilepsy.

3. Our results do not show any striking correlation between the mode of onset and the type of epilepsy, the intelligence quotient of the patient, the family history or the course and severity of the disease. The single exception was a small group of patients whose condition was diagnosed as alcoholic epilepsy, in all of whom the initial manifestation was an abrupt (violent) convulsion.

4. There was a tendency to correlation between the mode of onset and the age at onset (milder onsets tended to occur in younger subjects).

5. Our figures tend to demonstrate a period of latency between the apparent basis of the lesion in the brain and the onset of attacks. In our group this interval had an average value of eighteen months, the individual times ranging from immediate onset to sixteen years. This latent period may be a "waiting period" until secondary factors appear.

SYMPATHECTOMY IN MAN

ITS EFFECT ON THE ELECTRICAL RESISTANCE OF THE SKIN

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AND
MAURICE LEVINE, M.D.
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Sympathectomy in animals (monkeys and cats) was found to produce a great and consistent increase in the electrical resistance of the skin, particularly on the foot pad. As the measurements of resistance were found to be useful in the animals for determination of the completeness of sympathectomy, the time required for regeneration after sympathectomy, etc. (Tower and Richter [1] and Richter [2]), further observations were made to determine whether sympathectomy has the same effect in man. These observations were made on fourteen patients with surgical sympathectomy performed for therapeutic purposes (migraine, neuralgia, Hirschsprung's disease and Raynaud's disease).

METHODS

Knowledge of the electrophysiologic behavior of the skin has been obtained almost exclusively from observations made on the palmar and dorsal surfaces of the hands. Accordingly, the present studies were confined to these areas.

Electrodes (pure zinc disks and a saturated paste of zinc sulfate and kaolin) applied to the palms and backs of both hands were held in place by means of adjustable clamps (Richter [3]). A very small direct current and a portable galvanometer (Levine [4]) were used, and the resistance offered by the skin was calculated separately for the palm and the back of each hand.

From the Psychobiological Laboratory of the Henry Phipps Psychiatric Clinic, the Johns Hopkins Hospital.

This article was prepared for inclusion in the issue (April 1937) of the ARCHIVES dedicated to Dr. Adolf Meyer but was received too late.

1. Tower, S. S., and Richter, C. P.: Injury and Repair Within the Sympathetic Nervous System: III. Evidence of Activity of Postganglionic Sympathetic Neurons Independent of the Central Nervous System, Arch. Neurol. & Psychiat. **28**:1149-1152 (Nov.) 1932.

2. Richter, C. P.: Pathologic Sleep and Similar Conditions Studied by the Electrical Skin Resistance Method, Arch. Neurol. & Psychiat. **21**:363-375 (Feb.) 1929.

3. Richter, C. P.: Brain **50**:216-236, 1927.

4. Levine, M.: Measurement of Electrical Skin Resistance, Arch. Neurol. & Psychiat. **29**:828-842 (April) 1933.

In unilateral sympathectomy the resistance of the skin on the intact hand served as a control; in bilateral operations the controls were either the preoperative resistance in the individual case or the average figures obtained under similar conditions from a group of normal persons.

The sympathectomies were performed in the department of surgery of the Johns Hopkins Hospital, for the treatment of neuralgia, Hirschsprung's disease, migraine and Raynaud's disease. Owing to the fact that sympathectomy is not often performed for these disturbances, only fourteen patients were available. However, we believe that the results were sufficiently consistent to establish a definite relationship in man between resistance of the skin and the sympathetic nervous system and to suggest the value of this method for the study of sympathetic disorders.

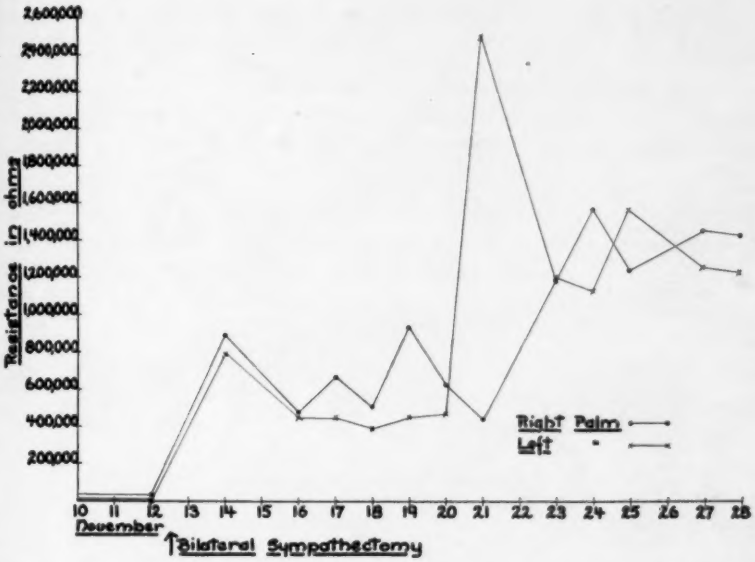

Chart showing the effect of bilateral sympathectomy on the electrical resistance of the skin of the palms.

RESULTS

Effect Produced on the Palmar Resistance.—Sympathectomies performed on ten patients were found to have effects similar to those produced in monkeys and cats. The palmar surfaces showed a large and consistent increase in resistance, while the dorsal surface showed in most instances a small and inconstant rise.

A typical record showing the effect produced by sympathectomy on the resistance of the skin on the palms of the hands is presented in the figure, with the resistance, expressed in ohms, indicated on the ordinates and the time expressed in days, on the abscissas. It will be seen that bilateral removal of the stellate and first thoracic ganglia through the dorsal approach was followed by an immediate increase in

the resistance of the skin from a level near 10,000 ohms to a level near 600,000 ohms. After eleven days it reached 1,400,000 ohms and was maintained there until the sixteenth day, when the patient left the hospital.

The results of these observations are summarized in the table. The average palmar resistance for four patients with unilateral removal of the stellate and the first thoracic ganglion on the left side was 889,060 ohms, as compared with 56,620 ohms on the right side, or a fifteenfold increase. In four patients with bilateral removal of the stellate and first thoracic ganglia, the resistance of 489,090 ohms on the right palm and

Data on Results of Sympathectomy on Electrical Resistance of the Skin

Name	Diagnosis	Postoperative Observation, Period of Days	Number of Records	Electrical Resistance of Skin, Ohms: Palmar or Plantar Surface, Right	Palmar or Plantar Surface, Left	Dorsal Surface, Right	Dorsal Surface, Left
Unilateral Cervical Sympathectomy Stellate and First Thoracic Ganglia							
W.	Migraine	10	4	102,750	942,250	330,000	270,000
C.	Sympathetic neuritis	12	12	49,340	344,000	197,080	422,580
Le B.	Migraine	5	4	39,400	525,000	315,000	359,400
W.	Sympathetic neuritis	2	1	35,000	865,000	245,000	635,000
	Average			56,620	889,060	271,770	421,740
Bilateral Cervical Sympathectomy Stellate and First Thoracic Ganglia							
I.	Migraine	19	11	878,630	979,540	683,180	1,192,270
P.	Sympathetic neuritis	6	5	327,000	327,000	511,000	215,000
P.	Migraine	1	1	475,000	445,000	415,000	385,000
H.	Chronic arthritis	26	13	275,760	119,610	840,380	575,760
	Average			489,090	467,790	612,390	592,000
Unilateral Lumbar Sympathectomy Left Second, Third and Fourth Lumbar Ganglia							
K.	Hirchsprung's disease	18	15	110,530	460,460	150,130	443,800
W.	Hirchsprung's disease	30	30	35,800	136,700	224,400	668,000
	Average			73,160	298,580	187,260	555,900

467,790 ohms on the left was markedly increased over the average of 35,750 ohms, obtained under similar conditions on ten normal persons. Unilateral removal of the second, third and fourth lumbar ganglia produced a definite, although much smaller, increase to 298,580 ohms on the left plantar surface, as compared with 73,160 ohms on the right.

In four patients for whom readings are not recorded in the table, removal of only the stellate ganglion through the ventral approach failed to produce any change in the resistance of the skin.

Effect Produced on the Dorsal Resistance.—It will be seen in the last two columns of the table that the resistance on the dorsal surface was irregularly affected by sympathectomy. In the four patients with left unilateral sympathectomy the average resistance was 421,740 ohms on

the left side and 271,770 ohms on the right. One patient showed a decrease on the side of operation. In the four patients with bilateral sympathectomy there was a small increase on both sides, to 612,390 ohms on the right and 592,000 ohms on the left. Both these readings were above the normal average of 220,000 ohms, obtained for ten normal persons. In two patients the resistance on the backs of the feet showed a definite increase to 555,900 ohms after lumbar sympathectomy.

COMMENT

It is evident from the experiments reported that the electrical resistance of the skin offers an excellent criterion for the effects of sympathectomy. The method has the advantage of simplicity and easy repetition, with little trouble to either the patient or the observer; it should be as useful in man as it has been in animals for determining the completeness and the extent of sympathectomy and, in instances of transection of white rami, the time required for the regeneration of sympathetic nerves.

Sporadic attempts have already been made to use this method for the evaluation of injuries and other disturbances in the sympathetic chain. Minor [5] reported an increase in the resistance of the skin on the forehead in nine soldiers with war injuries of the cervical portion of the sympathetic chain and a decrease in two patients in whom there apparently was irritation of sympathetic nerves; Richter [3] reported the case of a patient with a unilateral tumor in the thoracic region, with increase in the resistance of the skin of the hand on the affected side. That the method may be significant also in the study of more centrally located sympathetic phenomena is suggested by the marked changes in the resistance of the skin found in narcolepsy as well as in normal sleep (Richter [6]).

Changes produced in the electrical resistance of the skin on the palms are of most interest because of their great magnitude and constancy; they reflect to a large extent, if not entirely, changes produced in the sweat glands. The fact that the palmar resistance is capable of such great fluctuation suggests that sweat glands may function through a much wider range than is commonly believed.

The changes produced in dorsal resistance, although less great and less constant, are also of interest and value. Dorsal resistance undoubtedly is representative to a great extent of the skin on all parts of the body containing comparatively few sweat glands. In preliminary experi-

5. Minor, L.: Ztschr. f. d. ges. Neurol. u. Psychiat. **85**:482-507, 1923.

6. Richter, C. P.: Bull. Johns Hopkins Hosp. **45**:56-74, 1929; High Electrical Resistance of the Skin of New-Born Infants and Its Significance, Am. J. Dis. Child. **40**:18-26 (July) 1930.

ments we have found that in some patients the changes in the resistance of the skin on the arms, the chest, etc., seem to be sufficiently great to make possible a fairly accurate localization of the sympathetic lesion. By placing patients in a cool temperature, these differences can be made even more marked. It should therefore be possible by this method to estimate not only the extent of the lesion but the degree to which each area of skin is affected by sympathectomy.

SUMMARY

1. Cervical sympathectomy (removal of the stellate and first thoracic ganglia) in ten patients consistently produced a large increase in the electrical resistance of the skin of the palms of the hands.

2. Cervical sympathectomy produced a smaller and less consistent increase in the electrical resistance of the skin on the backs of the hands.

3. Lumbar sympathectomy (removal of the second, third and fourth lumbar ganglia) in two patients produced similar changes in the resistance of the skin on the soles and the backs of the feet.

4. It was concluded that readings of the electrical resistance of the skin should be as useful for the study of sympathetic disturbances in man as they have proved to be in monkeys and cats. This method has the advantage over others in that it requires little time and can be repeated at frequent intervals, with little inconvenience either to the patient or to the observer.

ASSOCIATION OF CAROTID SINUS REFLEXES WITH SYNCOPE AND CONVULSIONS

REPORT OF FOUR CASES

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Since the work of Hering in 1923 on the reflex control of the heart rate and the vasomotor system, there has arisen a new interest in a subject which has occupied clinicians for many years. In 1799 Parry,[1] in the course of a study on angina pectoris, noted that pressure on the neck slows the rate of the heart. Czermak[2] in 1866 observed in himself that pressure on an expansile body at the upper border of the sternocleidomastoid muscle resulted in retardation of the pulse. He thought that this effect was due to mechanical excitation of the vagus nerve. For many years clinicians accepted this explanation, even though a great deal of experimental work tended to disprove Czermak's conception. Pagano[3] in 1900 conducted experiments to show that the changes in the heart rate and vasomotor tonus produced by arterial hypotension or hypertension in the cerebral circulation are due not to a direct cerebral effect but to a reflex mechanism, the origin of which he localized to the bifurcation of the common carotid artery. Siciliano[4] in 1900 stated that the common carotid arteries are a protective mechanism against sudden anemia or hyperemia of the brain. Sollmann and Brown[5] noted that traction on the cephalic end of the common carotid

Read at a meeting of the Chicago Neurological Society, May 21, 1936.

1. Parry, C. H.: An Inquiry into the Symptoms and Causes of the Syncope Anginosa, Commonly Called Angina Pectoris, London, Cadell & Davis, 1799, p. 167.

2. Czermak, Joseph: Mechanical Irritation of the Vagus Nerve in Man, Jenaische Ztschr. f. Med. u. Naturw. **2**:384, 1866.

3. Pagano, in Heymans, C.; Bouckaert, J. J., and Regniers, P.: Le sinus carotidién et la zone homologue cardio-aortique, Paris, Gaston Doin & Cie, 1933.

4. Siciliano, in Heymans, C.; Bouckaert, J. J., and Regniers, P.: Le sinus carotidién et la zone homologue cardio-aortique, Paris, Gaston Doin & Cie, 1933.

5. Sollmann, T., and Brown, E. D.: The Blood Pressure Fall Produced by Traction on the Carotid Artery, Am. J. Physiol. **30**:88, 1912.

artery in animals produces a drop in blood pressure, slowing of the pulse and an increase in the respiratory rate. The change in the blood pressure was unaffected by section of the vagus nerves.

Hering [6] and his associates, notably Koch,[7] demonstrated that the vasomotor and cardio-inhibitory phenomena observed during the so-called *Vagusverdruck* are reflex in nature and originate from the carotid sinus. They showed that procainization abolishes the reflex and that direct stimulation of the vagus nerve is ineffective. They noted that the reflex can be obtained in the majority of elderly persons, especially in patients with a high degree of arteriosclerosis and hypertension. The effect is equal on the two sides. Koch pointed out that in certain patients the administration of digitalis seems to sensitize the carotid sinus, so that a marked response is obtainable.

Blanton and Blanton [8] reported the case of a patient who suffered attacks of syncope with convulsions, the onset of which was associated with buttoning his collar. They expressed the belief that this was a vagus effect, since they could reproduce the attacks, which were always accompanied by complete stoppage of the heart, by pressure supposedly on the vagus nerve.

Budde [9] stimulated the exposed carotid sinus in man and recorded a drop in blood pressure.

Roskam [10] reported the case of a man aged 53 in whom syncopal attacks were associated with manual compression of the carotid sinus while his collar was being buttoned. The syncope was associated with prolonged asystole of the heart. Weiss and Baker [11] and Ferris, Capps and Weiss [12] reported the histories of a series of patients in whom syncopal attacks were shown to be due to reflexes originating from the carotid sinus. The authors pointed out that in these patients the carotid sinus was unduly sensitive. The association of a syncopal attack during

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6. Hering, H. E.: Experiments with Pressure on the Carotid Sinus, München. med. Wchnschr. **70**:1287, 1923.

7. Koch, E.: Clinical Observations in Cases of Pressure on the Carotid Sinus, München. med. Wchnschr. **70**:1316, 1923.

8. Blanton, H. W., and Blanton, W. B.: Cardiac Standstill with Syncope Following Pressure on Right Vagus, J. A. M. A. **76**:1220 (April 30) 1921.

9. Budde, M.: Surgical Experiences with Carotid Sinus Pressure Experiments, Ztschr. f. d. ges. exper. Med. **50**:207, 1926.

10. Roskam, Jacques: A New Syndrome, Severe Cardiac Syncopes and Repeated Syncopes Due to Hyperreflexia of the Carotid Sinus, Presse méd. **38**: 590 (April 30) 1930.

11. Weiss, S., and Baker, J. P.: The Carotid Sinus Reflex in Health and Disease, Medicine **12**:297, 1933.

12. Ferris, E. B., Jr.; Capps, R. B., and Weiss, S.: Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions, Medicine **14**:377, 1935.

pressure on the carotid sinus with spontaneous hypersensitivity of the carotid sinus was also described by Moses and Feinstein [13] and by Smith and Moersch.[14]

Since the work of Weiss and his co-workers [15] indicating that certain persons with a clinical history of syncope and epileptiform seizures have an etiologically related hyperirritable carotid sinus, isolated reports [16] confirming their findings have appeared in the American literature. We are reporting here the histories of four patients [17] whom we have observed in the past eight months.

REPORT OF CASES

CASE 1.—M. Y., a Bohemian man aged 56, entered ward 64 of the Cook County Hospital, in the service of one of us (L. H. S.), on Nov. 7, 1935, with a history from the son that he had always been in good health until six weeks before his admission. At that time he began to experience spells of weakness, always when he was in the erect position, causing him to fall to the floor. There was no syncope or convulsions. Twelve days before his admission to the hospital, the patient experienced a "fainting spell" which lasted three minutes, after which he crawled to bed, where he felt well. On the day of his admission to the hospital the patient while at home fell to the floor in a sudden attack, during which he became unconscious and had involuntary defecation and urination. Convulsive movements were observed. He soon recovered from the attack, rose and walked about. He walked to and into an ambulance, rode to the hospital and walked into the receiving room, where he suddenly experienced another spell of weakness and lost consciousness. The past history was without significance, and there was no history of venereal disease.

Examination.—The patient appeared well developed and well nourished. He was in coma. The blood pressure was 162 systolic and 92 diastolic. The respiratory rate was 20, the temperature 101 F. and the pulse rate 92, with irregular rhythm. There was no rigidity of the neck. The pupils were widely dilated but reacted to light. The heart and lungs were normal. All four extremities were spastic, and a Babinski, Oppenheim and Rossolimo signs were elicited on both sides. Ankle clonus was present bilaterally. Spinal puncture at this time revealed normal fluid, except for 9 cells per cubic millimeter. During the course of the puncture the patient recovered from coma and spoke to his son in an intelligent manner. Subsequent to the puncture, repeated neurologic examinations demon-

13. Moses, H. M., and Feinstein, S. S.: Reflex Hypersensitivity of the Carotid Sinus, Ann. Int. Med. **8**:1413, 1935.

14. Smith, H. L., and Moersch, F. P.: Syncope of Patients with Hypersensitive Carotid Reflexes: Attacks Reproduced by Cardiac Standstill Induced by Pressure on Carotid Sinus, Proc. Staff Meet., Mayo Clin. **10**:401 (June 26) 1935.

15. Weiss and Baker.[11] Ferris, Capps and Weiss.[12]

16. Moses and Feinstein.[13] Smith and Moersch.[14]

17. We have seen eight additional cases, all similar to case 2, of the cardiac type. Two of the patients had the initial attack of syncope and convulsions after a surgical procedure—one, after removal of a specimen from the thyroid for biopsy, and the other, after a gynecological operation. The others had had attacks of syncope and convulsions for varying periods.

strated no obvious pathologic condition of the central nervous system. The blood pressure was 110 systolic and 60 diastolic, and the heart rate was 50, with regular rhythm.

An electrocardiogram revealed a sinus rhythm, with a rate of 50, a moderate degree of myocardial damage and left axis deviation. The urine was normal. The hemoglobin content was 90 per cent, the red cell count 4,500,000 and the white cell count 7,000, with 70 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes, 6 per cent monocytes and 1 per cent basophilic leukocytes. The Wassermann reaction of the spinal fluid and blood were repeatedly negative. The urea nitrogen content of the blood was 28.28 and 14 mg. per hundred cubic centimeters, respectively, in two determinations. The creatinine concentration was normal. The basal metabolic rate was plus 12 and 18 per cent, respectively, on two occasions. Roentgen examination revealed no changes in the stomach, duodenum or lungs. The heart was slightly enlarged. There were no demonstrable changes in roentgenograms of the skull.

Course.—During his sojourn in the ward, the patient had many attacks of loss of consciousness, both with and without convulsive movements. In one of these attacks he sustained a laceration of the forehead. It was noted that the seizures apparently were precipitated by change of posture, and this gave rise to the supposition that the attacks were related to postural hypotension. However, we were never able to induce an attack by change of posture alone, although we could precipitate a marked drop in blood pressure. Momentary pressure on the right carotid sinus or more strenuous pressure on the left, with the patient in the sitting position, gave rise to a definite sequence of events, which we were able to reproduce constantly; thus, there were immediate pallor of the face and a slight increase in the respiratory rate, followed by loss of consciousness. The blood pressure dropped to a low level. About eight seconds after the patient lost consciousness, there were tonic, followed by clonic, movements of the extremities and body. There was voidance of urine and feces. During the attack, the ankle and the patellar clonus were present.

Electrocardiograms showed a slowing of 12 beats during the seizure. Procainization of the right carotid sinus resulted in prompt hypertension of 24 mm. of mercury and complete cessation of the attack. The left carotid sinus was reactive. Procainization of the left carotid sinus gave similar results. A tight binder placed on the legs and abdomen elevated the blood pressure when the patient was in the sitting position, and he had symptoms of weakness, which soon passed off. Momentary pressure on each sinus individually (with the binder on) gave the immediate response as we previously had always observed it. The oculocardiac reflex, hypernictitation, hyperventilation and hydration with pitressin produced no seizures. Compression of the common carotid artery produced no changes in the level of the blood pressure, and the patient had no symptoms. Atropine sulfate in doses of $\frac{1}{50}$ grain (0.0013 Gm.) intravenously, as well as ephedrine sulfate in doses of $\frac{3}{8}$ grain (0.0243 Gm.) four times a day, had no effect on the induced attacks of unconsciousness with convulsions. Subcutaneous injection of 1 cc. of a 1:1,000 solution of epinephrine hydrochloride abolished the effects from both carotid sinuses and caused a rise in blood pressure of from 130 systolic and 80 diastolic to 190 systolic and 110 diastolic. On Dec. 11 the right carotid sinus was denervated by Dr. Adrien Verbrugghen. During the operation no changes in blood pressure were noted. However, one hour after operation the blood pressure rose to a level of 170 systolic and 90 diastolic, with the patient in the supine position. This persisted for one hour, without any change in the pulse or respiration. Repeated readings of the blood pressure thereafter

revealed a return to the normal level. Recovery was uneventful. Many examinations since have revealed total inactivity of the right carotid sinus. The sinus on the left was still active. The patient felt so improved that we could no longer keep him in the hospital for study. In the five months since the operation the patient has had no attacks.

CASE 2.—I. G., a white man aged 65, entered ward 64 of the Cook County Hospital on Feb. 10, 1936, with the history that he had always been in good health until 2 p. m. on the day of admission. He was sitting comfortably in a chair, when suddenly he arose, his face blanched and he fell to the floor unconscious. His body stiffened, and there were jerky movements of all the extremities. Almost as soon as he was recumbent, he seemed to be recovered, spoke to the persons present, got up and immediately fell again in another attack.

Examination.—The patient was alert and not acutely ill. The temperature was 97.8 F., the respiratory rate 26 and the pulse rate 88 with regular rhythm; the peripheral vessels were moderately sclerotic. The blood pressure was 150 systolic and 90 diastolic. There were an abrasion over the left eye and an ecchymosis covering the left upper lid. The pupils were regular and equal in size and reacted to light and in accommodation. The optic disks were normal; the retinal vessels showed a slight degree of sclerosis. The cranial nerves were intact. The right carotid sinus was prominent. The heart was not enlarged; the tones were normal; the rhythm was regular, and there were no murmurs. Expansion of the lungs was good; resonance, tactile fremitus and the breath sounds throughout were normal. No masses were palpable in the abdomen. The abdominal reflexes were intact; the extremities revealed no evidence of motor weakness or disturbances in sensation. The reflexes were physiologic. Spinal puncture revealed normal pressure, clear fluid and a negative reaction to the Pandy test; there were from 2 to 3 cells per cubic millimeter. The Wassermann reactions of the spinal fluid and blood were negative.

A Mosenthal test gave results within normal limits. The urine was normal. The urea content of the blood was 16.35 mg. Roentgen examination revealed no cardiac enlargement and no pathologic condition in the lungs. The initial electrocardiogram revealed slight evidences of myocardial damage. The hemoglobin content was 80 per cent (Tallqvist); there were 4,200,000 red cells and 7,200 white cells, with 65 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes and 2 per cent monocytes.

Slight pressure on the right carotid sinus resulted in immediate pallor of the face and loss of consciousness, followed by a latent period and then convulsions of a generalized clonic nature. Observations made as controls, such as pressure on the eyeballs of from six to seven minutes' duration, had no effect on the heart rate or the blood pressure, and the patient had no symptoms. Hypernictitation, hyperventilation and hydration with pitressin were without result. Pressure on the common carotid artery below the carotid sinus resulted in a slight increase in the rate of the heart, with a slight decrease after pressure was released. Electrocardiograms taken during an attack revealed stoppage of the heart for eight or ten seconds. The left carotid sinus was not as irritable as the right, but stronger and more prolonged pressure resulted in the same phenomena as with pressure on the right carotid sinus. Procainization completely abolished the reflexes on the right side. Spinal punctures revealed that even during asystole and syncope there was a rise in the spinal fluid pressure. In two attempts we were unable to produce a fall in the spinal fluid pressure during mechanical excitation of either the right or the left carotid sinus.

One and a half minims (0.092 cc.) of a 1:1,000 solution of epinephrine hydrochloride injected into the right common carotid artery by Dr. Adrien Verbrugghen abolished the reflex on that side. The right side of the face was blanched and the right pupil dilated. The blood pressure rose momentarily from 130 systolic and 80 diastolic to 160 systolic and 90 diastolic.

Subcutaneous injection of 1 cc. of a 1:1,000 solution of epinephrine hydrochloride resulted in a rise of 20 mm. in the systolic pressure, but stimulation of the carotid sinuses quickly induced the attack. However, the intravenous injection of 3 minims (0.184 cc.) of a 1:1,000 solution of epinephrine hydrochloride abolished the carotid sinus reflexes and the ability to induce an attack. Many electrocardiographic observations showed that about one and a half minutes after the epinephrine hydrochloride had been injected, multiple ectopic ventricular and auricular beats arose. These took the form of multiple ventricular extrasystoles, occurring singly or in paroxysms resembling ventricular tachycardia, and also many paroxysms of nodal as well as auricular extrasystoles. There were periods in which nodal rhythm was present.

Atropine sulfate in doses of $\frac{1}{50}$ grain (0.0013 Gm.) intravenously completely abolished the cardio-inhibitory findings, but a vasomotor effect was still evident. Ephedrine sulfate in doses of 1 cc. of a 1:1,000 solution subcutaneously and intravenously was ineffective in abolishing the reflex. The blood pressure constantly dropped from 130 systolic and 90 diastolic to 90 systolic and 60 diastolic during mechanical stimulation of the carotid sinuses. It was possible to produce contralateral convulsive movements without loss of consciousness, as well as generalized convulsive movements, and also varying degrees of disturbance in intracardiac conduction by varying the onset and severity of pressure on the carotid sinus.

Case 3.—J. G., a white man aged 65, entered ward 64 of the Cook County Hospital on Dec. 7, 1935, complaining of fainting spells for the past two years, tingling in the fingers for the past year and a half, cough for three weeks, fever and night sweats for the past week and weakness for the past four days. The patient stated that until two years before his admission he had been well. At that time, while painting the ceiling in a house, he fell and lost consciousness. He was taken home and felt dazed and weak. The next day he felt fine. Since, he had had about one attack every month until the Saturday before his admission to the hospital, when he had had three attacks in one day. The attacks were not related to meals but seemed to be associated with exertion. Several spells occurred while the patient was walking in the street. There were no convulsions. He complained of occasional palpitation of the heart. His appetite was poor, and he had lost 15 pounds (6.8 Kg.) in weight in the last year. There was no history of any venereal disease. Cholecystectomy had been performed in 1915.

Examination.—The patient was well nourished; he was lying in bed and was not acutely ill. The temperature was 99.4 F. and the pulse rate 82 with regular rhythm; the peripheral vessels were slightly sclerotic; the respiratory rate was 25 and the blood pressure 130 systolic and 80 diastolic. The pupils were equal and reacted to light and in accommodation. The fundi were normal. The pharynx was injected. The chest was emphysematous, and there were sibilant and sonorous râles throughout both pulmonary fields. The borders of the heart were difficult to outline; there were no murmurs; the rhythm was regular, and the second aortic tone was loud and ringing. Neurologic examination gave normal results.

Pressure on the right carotid sinus produced a sensation of weakness, spots before the eyes and a feeling of faintness, followed by loss of consciousness but no

convulsions. The left carotid sinus was inactive. The patient was under observation nineteen days. He had spontaneous attacks, which occurred, as had many of the others, while no one was around.

The Wassermann reaction of the blood was negative. Examination of the sputum for tubercle bacilli gave negative results. Roentgen examination revealed slight cardiac enlargement and slight increases of the right hilar markings. An electrocardiogram was normal. The urine was normal. The hemoglobin content was 80 per cent (Tallqvist); there were 4,500,000 red cells and 9,500 white cells, with a normal differential count.

Course.—It was not always possible to induce syncope by pressure on the right carotid sinus, although the premonitory symptoms could always be produced. Blood pressure readings taken during mechanical excitation of the right carotid sinus always revealed a rise of from 10 to 15 mm. of mercury in the systolic blood pressure. The pulse rate never changed. Procainization of the right carotid sinus abolished not only the induced attack but the premonitory symptoms and the rise in blood pressure. Injection into the right glossopharyngeal nerve of procaine hydrochloride by Dr. Adrien Verbrugghen resulted in anesthesia of the posterior third of the tongue on the right side and loss of ability to induce the attack but had no effect on the blood pressure. Unfortunately, the patient would not allow the procedure to be repeated. Procaine hydrochloride instilled into the carotid sheath below the carotid sinus was without effect. Pressure on the eyeballs, as well as pressure on the carotid artery below the carotid sinus and on isolated spots in the neck, had no effect on the blood pressure and produced no symptoms. Hyperventilation and hypernictitation produced no changes. Intravenous injection of 4 minims (0.25 cc.) of a 1:1,000 solution of epinephrine hydrochloride and 1/50 grain (0.0013 Gm.) of atropine sulfate did not prevent the induced attacks. The patient did not know what was being done. We carefully avoided suggestion. He refused to allow us to denervate the right carotid sinus.

Case 4.—M. J., a white woman aged 63, who was born in Bohemia and had lived in Chicago since 1896, entered ward 20 (oral surgery) of the Cook County Hospital on Nov. 25, 1935. She stated that she had always been in good health until about one year before admission. At that time she noticed a small, painless lump in the right side of the neck, below the angle of the jaw. This had progressively increased in size. The swelling in the right submaxillary triangle was discrete, firm and movable. There was no swelling in the floor of the mouth. The patient went home the next day.

She returned on Dec. 4, 1935, stating that the swelling was larger. It was then the size of a hen's egg. A roentgenogram of the jaw revealed no calculi and no involvement of the bone. On December 5 the mass was removed. Histologic examination revealed lymphosarcoma. The postoperative course was smooth and uneventful. Four days later, while the sutures and drain were being removed, the patient suffered a series of generalized epileptiform convulsions, with loss of consciousness, lasting five minutes. Neurologic examination by Dr. A. Ettleson revealed no involvement of the central nervous system to account for the seizure.

The additional history was obtained from the daughter that for the past fourteen months the patient had had spells of weakness, dizziness, spots before the eyes and unconsciousness, lasting from one to three minutes. It was noted that these attacks came on when she was in the sitting or standing position and that lying down would prevent them. Often, however, the patient could not get to a sofa or bed, and loss of consciousness followed. We could not determine whether the attacks occurred during rotation of the head.

Examination.—The patient was obese, with no evident loss of weight. There was a small amount of retinal arteriosclerosis. The lips were slightly cyanotic and suffused. There was no injection of the palate, nor was the tongue beefy red. An incision in the right side of the neck was indurated and tender. The right and left carotid sinuses were easily palpable. The chest was emphysematous, and the respiratory movements were shallow. The lungs were resonant; the expiratory phase of the breath sounds was prolonged, and there were no râles. The heart was enlarged to the left; the sounds were clear, although somewhat distant; the second aortic tone, as well as the second pulmonic tone, was accentuated; there were no murmurs, and the cardiac rate was from 80 to 90, with regular rhythm. The spleen was not palpable. There were no palpable glands in the axillary, inguinal, epitrochlear or left cervical regions.

A roentgenogram of the chest revealed an enlarged, aortic-shaped heart and some increase in the hilar markings. The urea nitrogen content of the blood was 18.15 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The urine was normal. An electrocardiogram revealed only slight evidence of myocardial degeneration and left axis deviation. A complete blood count revealed: hemoglobin content 113 per cent (Sahli), red cells 6,430,000 and white cells 14,750, with a differential count of 64 per cent polymorphonuclear leukocytes, 4 per cent eosinophils, 25 per cent lymphocytes and 7 per cent monocytes.

Course.—The blood pressure taken in the right and left arms, with the patient in the sitting, standing and supine position, was 190 systolic and 110 diastolic. Pressure on the right carotid sinus (Jan. 5, 1936) revealed no change in the blood pressure, pulse or respiration. The patient had no symptoms. Mechanical irritation of the left carotid sinus (with the patient in the sitting position) revealed a drop in blood pressure from 190 systolic and 110 diastolic to 144 systolic and 100 diastolic. The cardiac rate slowed from 90 to 62 beats per minute. The patient complained of weakness and dizziness. In the five months since the operation the patient has been well and has had no spells of any kind, nor have we been able to produce any attacks by pressure on the right carotid sinus. However, the last examination (May 7) revealed that the vasomotor and cardio-inhibitory phenomena associated with compression of the carotid sinus have returned on the right side. Thus, there were a drop in blood pressure from 190 systolic and 110 diastolic to 168 systolic and 100 diastolic and a slowing in the cardiac rate of 26 beats per minute.

COMMENT

The association of attacks of loss of consciousness and cardiac disturbances, such as asystole,[8] transient ventricular fibrillation complicating heart block[18] and paroxysmal tachycardia,[19] is well known. The relationship of the carotid sinus reflexes, as well as other reflexes originating from the throat and esophagus,[20] to syncope and convulsions has only recently been described.

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18. Schwartz, S. P.: Transient Ventricular Fibrillation, Arch. Int. Med. **49**:282 (Feb.) 1932; **50**:450 (Sept.) 1932.

19. Willius, F. A.: Clinic on Paroxysmal Tachycardia (Nodal Type), Pulmonary Tuberculosis and Thoracoplasty, Proc. Staff Meet., Mayo Clin. **10**: 759 (Nov. 27) 1935.

20. Weiss, S.; Ferris, E. B., Jr., and Capps, R. B.: Influence of Reflexes in the Induction of Intracardiac Disturbances, Tr. A. Am. Physicians **49**:177, 1934.

Weiss and Baker [11] and Ferris, Capps and Weiss [12] have shown that the carotid sinus may be the source of reflexes resulting in syncope, with or without convulsions. They divided the syncopes arising from the carotid sinus into three groups: (1) cerebral, (2) cardiac and (3) vasomotor. In the cerebral type mechanical irritation of the carotid sinus results in syncope, with no, or minor, vasomotor or cardiac disturbances. We have described one case of this type. The patient was of a neurotic disposition. However, the fact that he injured himself during several syncopal attacks, the dramatic effect of procainization of the right carotid sinus, which abolished the constantly induced syncope, the negative effect of injections used as controls, as well as pressure on other spots in the neck, our constant effort to avoid suggestion and the absence of stigmas of hysteria seem to indicate that the induced syncopes were related to the carotid sinus. As was pointed out by Weiss and his co-workers, atropine and epinephrine have no effect in preventing the attacks in this particular type of syncope. Since our patient allowed us to procainize the glossopharyngeal nerve only once, we can draw no conclusions, although it seems that this procedure would be valuable as an additional control. The opinion was expressed by Weiss and others that the mechanism of this form of syncope may be due to anoxemia brought about by reflex vasoconstriction of the cerebral vessels. Lennox, Gibbs and Gibbs [21] measured the cerebral blood flow during induced carotid sinus syncope and found no slowing of the cerebral circulation, indicating that if there is vasoconstriction of the cerebral blood vessels it is not generalized. The pathways of this reflex are not known.

In cardiac and vasomotor syncopes the disturbances in intracardiac conduction, as well as the vasomotor phenomena, would seem to account for the induced syncope resulting from pressure on the carotid sinus. The relationship of convulsions to reflex intracardiac disturbances is interesting. We have seen several patients in whom convulsions of a generalized clonic type were associated with reflex asystoles of the heart of from ten to fifteen seconds' duration, the asystoles being induced by pressure on the carotid sinus. All these patients were conscious during the convulsive seizure. In the cases reported here the syncope always came shortly (from one to three seconds) after the onset of stimulation, whereas the convulsive seizures occurred later. Even in the patients in whom syncope was associated with asystole and hypotension, Lennox, Gibbs and Gibbs [21] found that the degree of cerebral circulatory slowing was not as marked as could be produced

21. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Relationship of Unconsciousness to Cerebral Blood Flow and to Anoxemia, Arch. Neurol. & Psychiat. **34**:1001 (Nov.) 1935.

by other procedures which did not result in loss of consciousness. It would seem that even in these patients the syncope may be associated primarily with the cerebral reflex.

Many cases of postural hypotension with syncopal attacks have been reported.[22] Ferris, Capps and Weiss [12] found only one of a group of four patients with postural hypotension who reacted to pressure on the carotid sinus. In the first patient whose case we have described, postural hypotension, although marked, did not result in syncopal attacks. However, pressure on either carotid sinus quickly induced loss of consciousness, followed by generalized clonic convulsions during which there was voiding of urine and feces. Koch [7] and Heymans and his associates [23] have shown that carotid sinus reflexes are most easily induced at or about the normal blood pressure of the animal species investigated. Heymans has found that in states of hypotension occlusion of the common carotid arteries, thereby producing hypotension in the carotid sinuses, results in a further drop in the blood pressure rather than the expected rise. It may be that in patients with marked postural hypotension any sudden additional lowering of the systemic blood pressure produced by exertion or sudden change of posture will result in stimulation of the carotid sinus, further lowering of the blood pressure, syncope and convulsions. In one other patient with postural hypotension and attacks of paroxysmal tachycardia, pressure on the carotid sinus resulted in immediate cessation of the tachycardia and restoration of the normal cardiac rate and rhythm.

In the fourth patient there was a definite association between the tumor in the neck and the attacks. Certainly, the fact that since the operation (five months) the patient has had no symptoms would speak in favor of this view. Furthermore, in Roskam's case and in many of the group reported by Weiss and his co-workers, syncope was associated with mechanical irritation in the region of the carotid sinus by a gland, stiff collar, sudden turning of the head, etc.

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It has been shown by Urban [24] and Weiss and Baker [11] that there is no known relationship of the carotid sinus reflex to various other common forms of convulsions. In epileptic patients whom we have seen, we have been unable to induce any form of attack by pressure on the carotid sinus. However, it must be pointed out that peculiar epileptiform attacks in elderly persons may be due to reflexes originating from the carotid sinuses. In the differentiation, the relationship of posture [25] to the attacks is important, for the syncope and convulsions due to hyperirritability of the carotid sinus usually occur when the subject is in the erect posture. Furthermore, the onset is slower, and in the patients we have observed the attacks are short and are not followed by any sequelae usually seen after the common epileptic seizure. Also, in these patients the attacks could not be induced by hyperventilation or hydration.

Aside from the removal of any local pathologic condition and the use of ephedrine sulfate or allied drugs in the cardiovascular type, the only therapeutic measure which has been attempted in this condition has been denervation of the carotid sinus. If the attacks are repeated and disabling, the more irritable of the two carotid sinuses may be attacked surgically. Although in animals it has been shown [26] that denervation results in transient hypertension (up to several months) and tachycardia, Danielopolu and Aslan,[27] Urban [24] and Weiss and his co-workers [15] have shown that in man hypertension and tachycardia following even bilateral denervation rarely last as long as a week. More recently, Dr. Paul Bucy [28] has shown that section of the glossopharyngeal nerve (which includes section of the nerve to the carotid sinus) results in hypertension lasting only from seven to ten days.

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In the one patient on whom surgical denervation of the right carotid sinus was performed by Dr. Verbrugghen, the elevation of the systolic blood pressure lasted only an hour.

SUMMARY AND CONCLUSIONS

1. Four cases of abnormal response to mechanical stimulation of the carotid sinus have been described.

2. The association of the carotid sinus with spontaneous syncope and convulsive seizures has been discussed. In a number of patients with attacks of weakness, vertigo, atypical epilepsy and vague epileptiform seizures, the carotid sinus reflex may be etiologically responsible. The diagnosis is based on the repeated induction of these attacks by pressure on the carotid sinus and the inability to produce them after procainization.

3. Attempts to raise the blood pressure by denervation of the carotid sinus in man are probably futile.

4. The practical importance of the carotid sinus in its relation to the differential diagnosis of epilepsy has been pointed out.

5. If the carotid sinus is found to be hyperirritable in patients with the symptoms described, local pathologic conditions in the region of the carotid sinus should be removed, if present, and denervation of the carotid sinus should be considered. In the cardiovascular group the epinephrine group of drugs may be used.

Miss Myrtle Sand, of the electrocardiographic laboratory of the Cook County Hospital, and Dr. Adrien Verbrugghen rendered valuable assistance in this study.

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DISCUSSION

DR. RICHARD CAPPS: I have been interested in hearing this paper, particularly because the authors included at least one case of the cerebral type of carotid sinus reflex. I think that the carotid sinus syndrome, although not exceptionally common, is important, for it can be cured or alleviated and the conditions with which it is associated are incurable. Epilepsy is usually the chief consideration for differential diagnosis, but distinction can be made at once by the fact that in cases of the carotid sinus syndrome one can reproduce the effects by compressing the carotid sinus, while in cases of epilepsy one can rarely, if ever, reproduce the attacks by this method. The attacks in connection with the carotid sinus syndrome rarely last more than two minutes, whereas epileptic seizures frequently last considerably longer. The diagnosis is also confused with narcolepsy and catalepsy. In cases of these two conditions in which we made examination we were not able to reproduce the attacks, although the clinical picture is similar to that in certain cases of hypersensitivity of the carotid sinus.

I wish to draw attention to the cerebral type of the carotid sinus reflex, that is, the form in which fainting occurs without significant change in the pulse or

the blood pressure. This reflex plays a rôle in many cases in which there is apparently a sufficient slowing of the pulse or fall in blood pressure to explain the symptoms. After atropinization the fainting occurs as quickly as before. This type of carotid sinus syncope is still thought by some observers to be hysterical in nature. However, procainization of the sinus abolishes the reflex, whereas application of a saline solution has no effect. Furthermore, pressure on any other part of the neck is without effect.

Finally, it is important to recognize the prodromal symptoms of fainting when actual loss of consciousness does not occur. Thus, patients may complain of attacks of unilateral paresthesias or unilateral twitching or even convulsions. In some cases unexplained dyspnea or sudden sweating, accompanied by a chilly sensation, may be the presenting symptoms. In all cases, if the carotid sinus is at fault, proper stimulation of the sensitive sinus will reproduce the symptoms exactly.

Dr. Paul C. Bucy: Attacks of syncope due to hyperactivity of the carotid sinus reflex are undoubtedly more common than is generally recognized. I was interested to learn that the authors abolished temporarily the induced attacks of syncope by the administration of epinephrine. Recently, through the courtesy of Dr. A. S. Alving, of the University of Chicago Clinics, I have had the privilege of observing an elderly attorney who suffered from attacks of syncope four or five times a day. Identical attacks could be produced by compression of the carotid sinus. Synchronously with the syncope there occurred a marked fall in the arterial tension and cessation of cardiac activity for three seconds. Ephedrine (25 mg., three times a day) was given. The spontaneous attacks of syncope ceased. Compression of the carotid sinus no longer caused as marked a fall in blood pressure as before, although the effect on the cardiac rate was unchanged.

The temporary arterial hypertension following unilateral intracranial section of the glossopharyngeal nerve (of which the nerve supplying the carotid sinus is a branch), which I described at a meeting of the Chicago Society of Internal Medicine in November 1935, has since been observed in other cases.

Dr. LeRoy H. Sloan: During the past several years I have had occasion to compress the carotid sinus in many cases, in an effort to terminate attacks of paroxysmal tachycardia. I have been impressed with the fact that many times one may almost step on the vagus nerve and the carotid artery below the sinus without any effect on the tachycardia but that when compression is properly applied to the carotid sinus itself, there is immediate cessation of the attack. When I examined the first patient whose case I have described, I was impressed by the almost certain specific relationship of the sinus to the attacks. I applied pressure suddenly to the right carotid sinus. There was a transitory change in respiration, and then there developed a convulsive attack, which began in the left arm. This observation of a contralateral jacksonian seizure during compression of the carotid sinus has been reported by others and has been made by Dr. Capps. On another occasion sudden compression of the carotid sinus resulted in a convulsive seizure, during which the patient showed typical epileptic reactions, including even urination and defecation.

In young patients one not infrequently sees a more obvious response to vagal, ocular or abdominal pressure than to pressure on the carotid sinus, while in older patients the reaction on compression of the carotid sinus is more definite. Recently we have had a patient with attacks of paroxysmal tachycardia. These attacks can be stopped instantly by compression of the carotid sinus area. However, the other day, when he arose from bed and started to walk across the ward, he

had an attack in which he fell and lacerated his scalp. On further examination we found that he had a marked drop in blood pressure on assuming the erect position. By compressing the abdomen with a scultetus binder and the legs from the ankle to the knee with elastic bandages, we could not only maintain the pressure at the same level with the patient in the erect position as in the supine position but could elevate it to over 200 mm. systolic and hold it there. I do not know that there is any direct relationship between the carotid sinus and postural hypotension, although such a relationship has been described. However, the suggestion is worthy of consideration. I have had two patients, each with a tumor of the vagus nerve, and I recall no symptoms manifested by these persons which even resembled those shown by our patients with sensitivity of the carotid sinus.

NECROTIZING ENCEPHALITIS

SIMULATING TUMOR OF THE BRAIN CLINICALLY AND DUE TO NECROTIZING ANGIITIS: A CLINICOPATHOLOGIC REPORT

NORMAN A. LEVY, M.D.

CHICAGO

Except in syphilis, primary inflammation of blood vessels, especially those of the central nervous system, is rare. It is recorded infrequently, and for this reason the clinical and pathologic data in an instance of such a condition are presented here.

REPORT OF A CASE

History.—A white boy aged 10 years was well until five months before his admission to the hospital. He had had pertussis at 8 months, measles at 11 months, chickenpox at 2 years and tonsillectomy at 3 years of age. At the age of 7 he received an injury to the head. Although he was unconscious for fifteen minutes, he recovered sufficiently to walk home unassisted. A roentgenogram taken soon afterward revealed no evidence of fracture of the skull. Two months later, however, he complained of supra-orbital headaches and dimness of vision in the left eye. The faulty vision was corrected with glasses, but the mild headaches continued intermittently for the next three years.

At the age of 9 he had an acute febrile illness, lasting eight days, which was characterized by severe sore throat, high fever and a spotty rash on the arms and legs. There was no subsequent desquamation. After this illness he suffered from frequent colds and "sinus trouble" and had frequent mild headaches in the frontal region.

The family history was essentially without significance, and there was no history of syphilis.

The terminal illness had a sudden onset five months before his admission, with a generalized convulsive seizure and loss of consciousness lasting five minutes. Four months before admission the parents noticed that the child's memory was not as good as formerly and that he was somewhat less active. The impairment of memory became progressively more severe and, until onset of the more acute symptoms just prior to admission, formed the outstanding feature of the illness. Two weeks before admission, he complained of headaches in the frontal region and vomited several times. One week prior to admission he had an attack of coma lasting one hour, followed by semistupor for twenty-four hours. During the following week he was somnolent and was admitted to the Mount Sinai Hospital on Oct. 2, 1934.

From the Division of Laboratories and the Neurological Service of Dr. Israel Strauss, the Mount Sinai Hospital, New York.

Read in part with Dr. Joseph H. Globus before the American Association of Neuropathologists, Montreal, Canada, June 5, 1935.

Read in part with Dr. Joseph H. Globus before the New York Neurological Society, New York, Oct. 1, 1935.

Examination.—On admission to the hospital the patient presented the habitus of the so-called Fröhlich type, with feminine distribution of fat and undescended testes. The temperature and pulse were normal. The blood pressure was 118 systolic and 80 diastolic. The heart and lungs were normal. The patient was somnolent and showed considerable intellectual impairment. There was a marked memory defect for both recent and remote events. There was considerable restlessness, with frequent scattered, patternless movements of the hands and feet. The right pupil was irregular and dilated, larger than the left and almost fixed to light and in accommodation. The left pupil was regular and smaller than the right; it reacted sluggishly to light and was fixed in accommodation. Vision was 20/70 in the right eye and 20/30 in the left; there was no papilledema. The ocular movements were normal, and there was no nystagmus. There was slight weakness of the lower part of the face on the left. The deep reflexes were active and equal, and there was a questionable Babinski sign bilaterally. The abdominal reflexes were present but diminished.

Course.—Shortly after admission a lumbar puncture revealed xanthochromic fluid containing 90 cells, all of which were mononuclears. The pressure fluctuated between 140 and 360 mm., but there was no evidence of a block. The sugar content of the spinal fluid was 50 mg. per hundred cubic centimeters; the chloride content, 725 mg., and the total protein content, 500 mg. The white cell count was 10,400, of which 40 per cent were polymorphonuclear leukocytes and 46 per cent lymphocytes. The red cells numbered 5,000,000, and the hemoglobin content was 92 per cent. The urine was essentially normal. The basal metabolic rate was minus 21 per cent. The Wassermann reaction was negative. The patient complained frequently of headache, and there was persistent bradycardia. Roentgenography of the skull showed a small sella turcica and no evidence of increased intracranial pressure.

On the seventh day after admission right homonymous hemianopia was noted, and subsequently right mimetic facial weakness and a tendency to a Babinski sign on the left appeared.

On October 11 encephalography was attempted but was discontinued after the withdrawal of 20 cc. of xanthochromic fluid, because the boy complained of difficulty in breathing. After this the memory defect became more severe, but there was no aphasia. On October 15 ventriculography was performed through the right occipital pole. Only 10 cc. of xanthochromic fluid escaped, and 50 cc. of air was injected. The roentgenogram showed a slightly dilated right ventricle and no air in the left (fig. 1).

It was thought that the patient had an expanding intracranial lesion, probably a suprasellar neoplasm or possibly, in consideration of the Fröhlich syndrome, a tumor of Rathke's pouch.

A second ventriculography, through the left occipital pole, was attempted on October 18. The operator was unable to find the ventricle, but a small piece of tissue was aspirated.

On October 22 craniotomy was performed in the left parieto-occipital region. The occipital convolutions appeared flattened, but no lesion was visible. The cortex was incised, and at a depth of 5 cm. a hard mass was encountered. This mass appeared to extend so far anteriorly that only partial removal by curettage was considered advisable.

Microscopic examination, by Dr. J. H. Globus, of the tissue removed at operation showed disintegrated brain tissue, in which there were perivascular infiltration

with mononuclear cells and moderate gliosis. No tumor tissue was seen. These observations were interpreted as indicating a reactive process in the vicinity of a massive lesion, which was probably neoplastic.

After the operation right hemiplegia, aphasia and complete amaurosis developed. The general condition became progressively worse; atrophy of the optic nerve developed slowly, and during the subsequent weeks the patient led a practically vegetative existence. There was low grade, intermittent fever, but the operative wound showed no signs of infection. About a month after operation the patient began to have involuntary hyperkinetic movements on the left side, and beginning bilateral papilledema, superimposed on the atrophy of the optic nerve was noted. The hyperkinetic movements, which soon involved both sides, became so pronounced that the patient had almost continuous convulsive

Fig. 1.—Ventriculogram, anteroposterior view, showing the dilated right ventricle and failure of the left ventricle to fill.

seizures. He died in status epilepticus, on November 22, one month after operation and seven weeks after admission. The terminal symptoms were interpreted as involvement of the basal ganglia by the neoplasm.

Observations at Necropsy.—Gross Anatomic Changes: The brain [1] was slightly larger than normal, and the convolutions were everywhere flattened. At the operative site the left temporoparieto-occipital region, which bulged markedly, consisted of disorganized, softened tissue. On sectioning the brain horizontally at various levels, the following abnormalities were noted: There were large areas of altered tissue, grayish pink and softer than normal, with many red and discolored spots of varying size (fig. 2). These pathologic areas had a strikingly symmetrical bilateral distribution; they extended anteriorly from the structures about the rostral portion of the third ventricle, involving bilaterally the corpus

1. Unfortunately, permission for a full autopsy was not granted, so that only the brain was available for pathologic study.

striatum, the thalamus and the posterior limb of the internal capsule, posteriorly into the occipital lobe, involving the regions adjacent to the posterior horn, and ventrally, deep into the temporal lobes. These large areas of altered tissue were bounded laterally by both islands of Reil and extended dorsally into both centra semiovale and into the gray matter of the right gyrus cinguli. A large area of disorganized brain tissue was present at the operative site, in the left temporoparietooccipital region, extending into the lateral ventricle on that side. Just lateral to, but not communicating with the right posterior horn were two large cavities, each about 1 cm. in diameter, containing blood clots. The ventricular system was markedly distorted. The third ventricle was practically obliterated and displaced to the

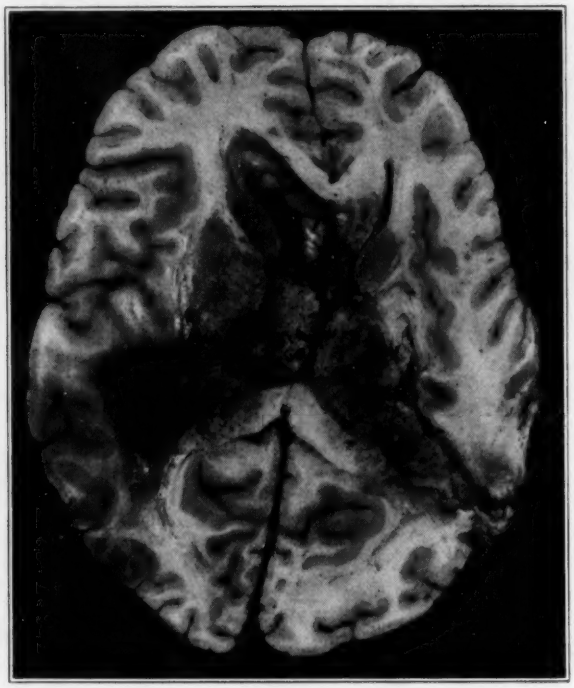

Fig. 2.—Horizontal section of the brain through the basal ganglia, demonstrating the distribution of the gross lesions.

left. The left anterior horn was narrowed; the right was dilated, and both were displaced to the left. Both posterior horns were narrowed, the right being almost completely occluded. The ependymal lining of the ventricles was yellowish and had a granular appearance. The tuber cinereum was markedly thickened and showed changes similar to those already described. Sections through various levels of the brain stem showed a few small discolored spots and small red streaks, particularly in the lateral portion of the left peduncle.

Microscopic Anatomic Changes: Sections taken from various regions of the brain and stained by the usual neuropathologic methods revealed widely disseminated inflammatory and necrotizing lesions but no evidence of neoplastic

disease. As the microscopic changes in the grossly diseased areas differed considerably from those in the adjacent and remote areas, the histologic alterations in these various regions will be described under separate headings.

Grossly diseased areas: These areas, most pronounced in and about the basal ganglia and in the vicinity of the posterior and inferior horns of the lateral

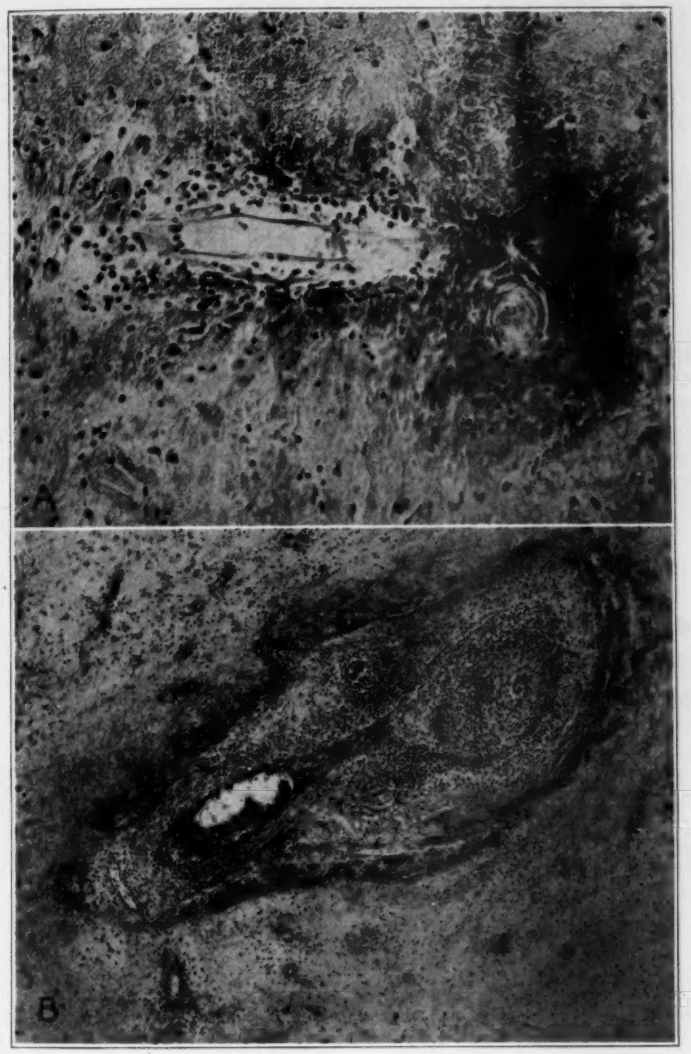

Fig. 3.—*A* (× 220) shows necrosis of the brain tissue and vessels, and *B* (× 66), necrosis, swelling and infiltration of the vessels. Hematoxylin and eosin stain.

ventricles, disclosed the most striking changes. In the sections of different parts of the massive lesions stained as a routine, there was extensive and profound necrobiosis of a peculiar coagulating type, affecting all the elements of the brain

tissue, so that, except for many diseased blood vessels, but few recognizable structures were visible (fig. 3 *A*). In the immediate vicinity of such vessels there were many areas of complete loss of tissue, appearing in the sections as unstained lacunae. The alterations in these areas affected the blood vessels, the neuroglia and the nerve cells in varying degrees and will be described under their respective captions.

Blood vessels: Both large and small vessels showed marked degenerative and inflammatory changes, in varying degrees (fig. 3 *B*). This was especially well demonstrated in the Weigert elastica and Van Gieson stains. Many of the vessels, especially the smaller, were converted into structureless, homogeneously staining, necrotic rings. Others, not so completely degenerated, showed swelling

Fig. 4.—Fibrin deposits in the parenchyma about a blood vessel. Weigert's fibrin stain; × 120.

of the intima, varying degrees of swelling and necrosis of the media and diffuse infiltration of all the coats with mononuclear and polymorphonuclear cells and a few red cells. In some of the necrotic vessels the internal elastic membrane was partially preserved, while in others it had completely disappeared. Many vessels, particularly the smaller ones, were seen in the Weigert fibrin stains to be partially or completely occluded by fibrin, and deposits of fibrin were observed in the surrounding tissues (fig. 4). There were also many perivascular hemorrhages, varying in size from microscopic to gross areas 1 cm. in diameter.

Neural elements: In gold and silver preparations there were visible only a few shadowy glia and nerve cells and a few broken, naked axis-cylinders, as

practically all the nerve cells, axis-cylinders and neuroglia were completely lost in the central parts of the necrotic areas. Near the periphery of the necrotic areas small numbers of intact nerve cells and axis-cylinders were present. Myelin preparations revealed marked loss and degeneration of myelin sheaths (fig. 5 *A*),

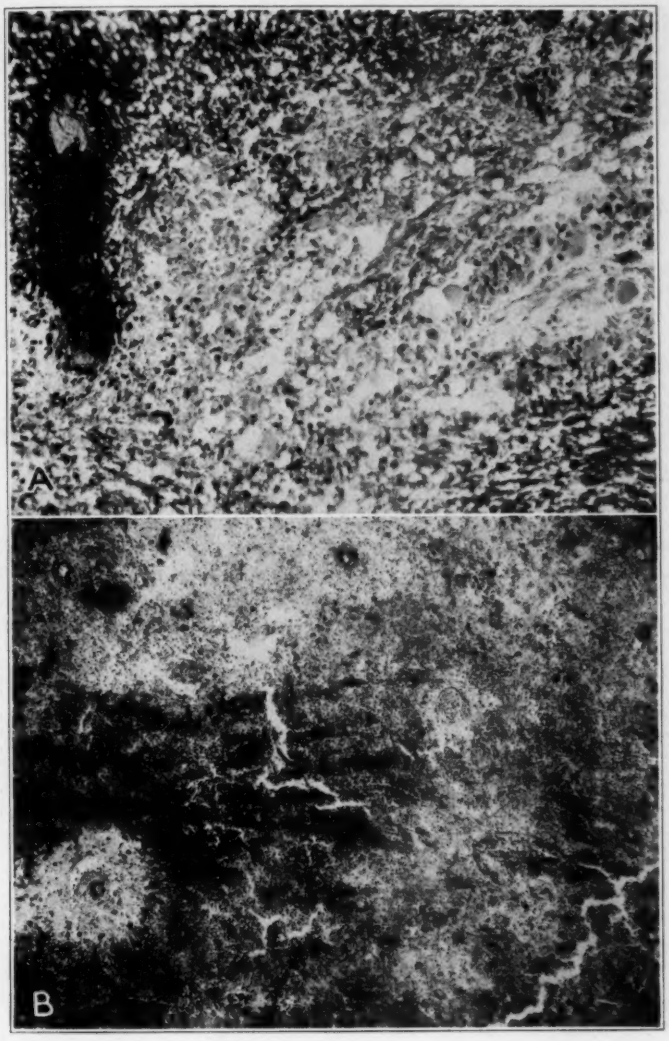

Fig. 5.—*A* (× 200) shows a small focus of recent destruction of myelin and *B*, (× 46) extensive demyelinization with pronounced perivascular distribution. Spielmeyer stain for myelin.

especially about the blood vessels. These patches of complete demyelinization, in the centers of which severely diseased or obliterated vessels were always observed, corresponded to the unstained perivascular lacunae observed in the

other sections (fig. 5 *B*). Around the periphery of these perivascular demyelinated areas were rows of round clumps of myelin globules. When sections were stained for fat by the Marchi or the Herxheimer scarlet red method and with the nile blue stains, heavy deposits of fat were seen in a similar distribution. These round

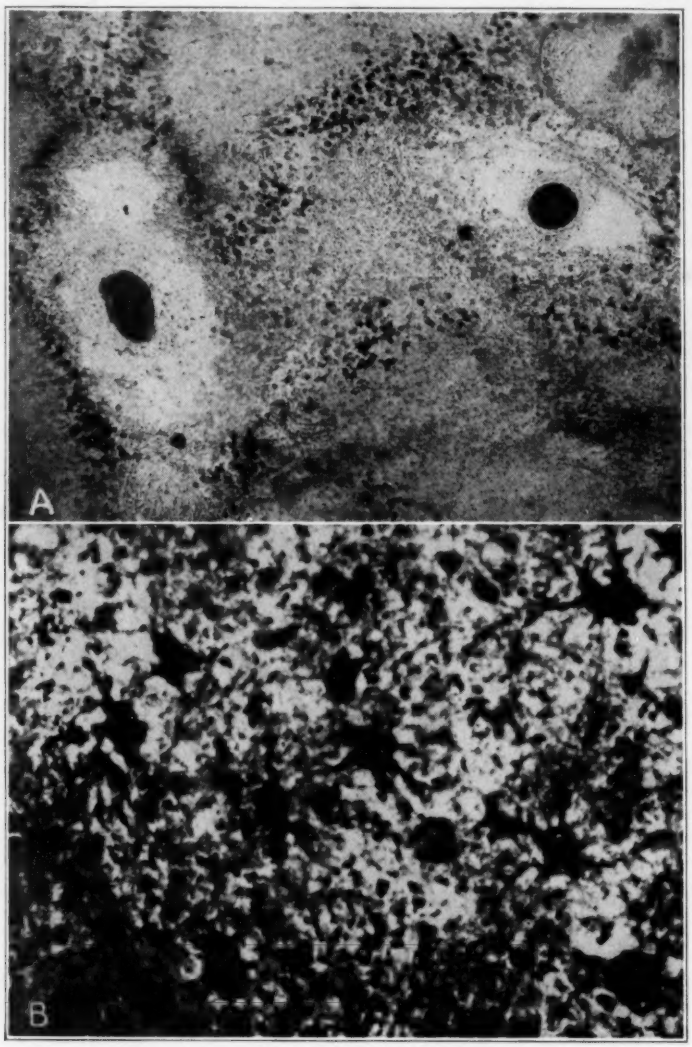

Fig. 6.—*A* (Marchi preparation; × 46) shows the distribution of clumps of fat about perivascular zones of necrosis, and *B* (Globus modification) of the Cajal gold sublimate method; × 520, hypertrophied macroglia cells undergoing clasmatodendrosis.

clumps of fat globules formed rows and collars about the edges of the most profoundly necrotic foci and joined similar adjacent rows, producing a striking mosaic appearance (fig. 6 *A*). Most of the fat was observed within compound

granular cells, although a small amount was seen lying free. The glial elements were also profoundly affected. In the central parts of the necrotic areas a moderate number of compound granular cells were seen distributed, for the most part, about the periphery of the perivascular necrotic zones, and there were small foci of softening containing gitter cells and mononuclear leukocytes. Micro-

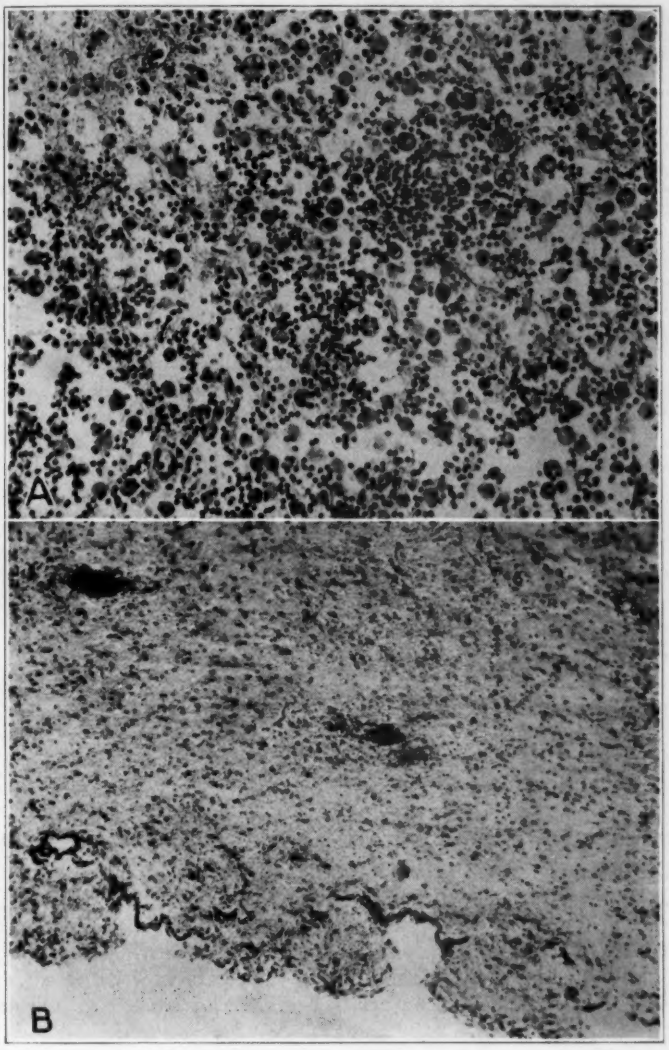

Fig. 7.—*A* (×200) shows a large focus of softening and cellular infiltration with inflammatory and glia cells, and *B* (×100), the wall of the third ventricle showing ependymal changes. Hematoxylin and eosin stain.

glia cells were not seen in the necrotic areas except in the smaller foci involving the cortex, where numerous hypertrophied microglia cells were undergoing

degenerative changes. A definite astrocytic reaction was present, especially toward the edges of the necrotic areas and in the subependymal zones. There, many large, swollen gemästete glia cells were seen, as well as groups of large astrocytes undergoing clasmatodendrosis (fig. 6 *B*).

Inflammatory changes: Throughout the necrotic areas there was a moderately severe inflammatory process consisting of infiltration of the walls of the vessels and the perivascular spaces with lymphocytes and mononuclear and polymorphonuclear leukocytes. The inflammatory cells infiltrated the parenchyma about many of the blood vessels, and in several places large areas were extensively infiltrated with mononuclears, plasma cells, macrophages and neuroglia cells (fig. 7 *A*). About some of the vessels were elongated cells, with bizarre-shaped nuclei—elongated, crescentic, hooked or dumb-bell-like. Many of the inflammatory cells were also affected by the necrotizing process and showed marked pyknosis. Appropriate stains failed to demonstrate micro-organisms in this inflammatory tissue. With Turnbull's blue stain no iron pigment was observed.

The aforementioned pathologic changes involved chiefly the basal ganglia and the white matter, but in a few places the necrotizing process involved the gray cortex also, as in the gyrus cinguli on the right. In addition, there was well marked ependymitis, characterized by numerous ependymal granulations, loss of the ependymal lining, foci of subependymal perivascular round cell infiltration and hemorrhages and areas of subependymal gliosis (fig. 7 *B*). The ependymitis was most pronounced in the third ventricle and the posterior and inferior horns of the lateral ventricles, but a few foci of perivascular round cell infiltration were also present about the aqueduct and beneath the floor of the fourth ventricle.

Zones adjacent to the grossly diseased areas: Examination of sections taken from the edges of the grossly diseased areas, where they merged with the macroscopically normal areas, revealed a transition from the condition characterized chiefly by necrosis to that consisting essentially of an inflammatory and a proliferative glial reaction. The parenchyma was relatively preserved, but the vascular and glial apparatus showed marked changes. The vessels on the whole were intact and showed little necrosis. The walls, however, were infiltrated with large and small mononuclear cells and a few polymorphonuclear cells (8 *A*). These cellular infiltrations frequently extended into the surrounding parenchyma.

Regions of the brain distant from the grossly diseased areas: Here the widely disseminated inflammatory and degenerative disease was limited almost entirely to the white matter. Small foci of perivascular round cell infiltration were observed in the occipital and temporal lobes and, to a less extent, in the frontal lobes. The white matter of the occipital and temporal lobes was rarefied and showed considerable diffuse demyelinization, and there was a diffuse deposition of fat globules lying free in the tissues. In these rarefied areas there was also an increase in the oligodendroglia cells, which showed a definite tendency to accumulate along the vessels. The macroglia cells, many of which were of the gemästete type (fig. 8 *B*), with abundant, pink-staining cytoplasm, were increased in number and showed degenerative changes, consisting chiefly of swelling of the cytoplasm and eccentricity of the nuclei (ameboid glia). Holzer preparations showed marked increase in glia fibers in these areas, forming small glial scars in places (fig. 9 *A*). A few small foci of softening containing macrophages and leukocytes were present. The gray matter was essentially normal. There was a low grade meningeal process consisting of slight infiltration of the meninges, especially in the depths of the sulci, with lymphocytes, macrophages and fibroblasts, dilatation and engorgement of some of the subarachnoid and subpial vessels, a few subpial hemorrhages and an increase in connective tissue. An occasional perivascular hemorrhage was

seen in the superficial cortex. The meninges overlying the necrotic areas, such as those in the gyrus cinguli, had also undergone marked degeneration and appeared almost hyalinized in places.

Brain stem: The inflammatory process involved the brain stem to a much less degree. Small foci of perivascular round cell infiltration were noted in the

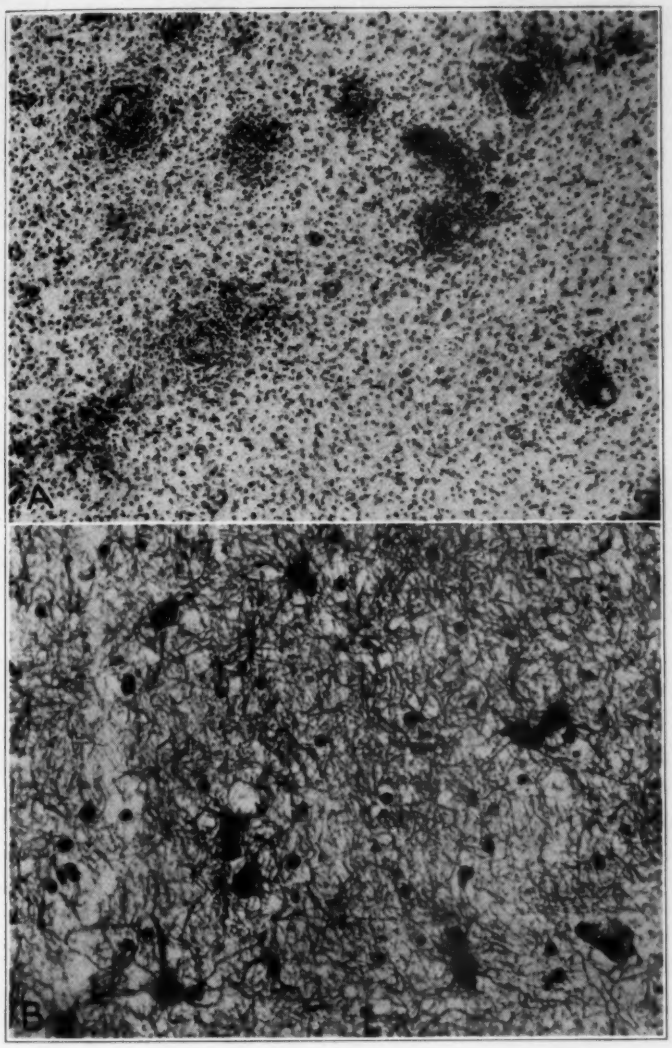

Fig. 8.—*A* (Nissl stain; × 120) shows inflammatory lesions at the edge of necrotic areas, and *B* (Holzer preparation; × 370), a section of the occipital lobe, with proliferation of the glia and increase of glia fibers in the white matter distant from the necrotic areas.

subthalamus, the tuber cinereum and the midbrain. The substantia nigra was free from disease changes, and only an occasional focus was observed in the

periaqueductal region. There were degenerative changes in the nerve cells and axis-cylinders in the subthalamus, although the inflammatory reaction was minimal. The nerve cells of the nuclei in the brain stem were normal except in the left lateral geniculate body, where the necrotizing inflammatory process had extended

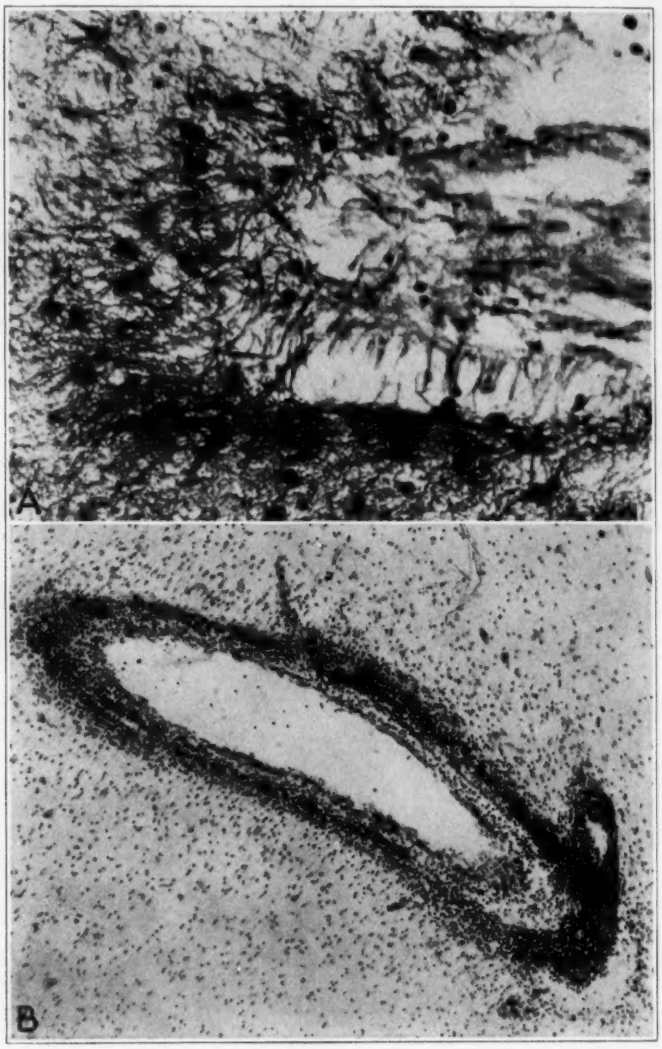

Fig. 9.—*A* (Holzer preparation; × 370) shows a section of the occipital lobe, with astrocytic proliferation and a glial scar near a blood vessel, and *B*, (Nissl stain; × 100), an inflammatory focus in the cerebral peduncle.

from the adjacent pulvinar of the thalamus. Circumscribed perivascular inflammatory foci were present in both cerebral peduncles (fig. 9 *B*). There was descending degeneration of the left pyramidal tracts, which could be traced

as far as the decussation of the pyramids. Degenerative changes in the nerve roots, demonstrated by small deposits of fat in Marchi preparations, and slight degenerative changes in the myelin sheaths with the Weil stain, were observed. A slight amount of fat was present in the posterior columns, limited chiefly to both fasciculi cuneati. Patches of a low grade meningitic process were noted along the

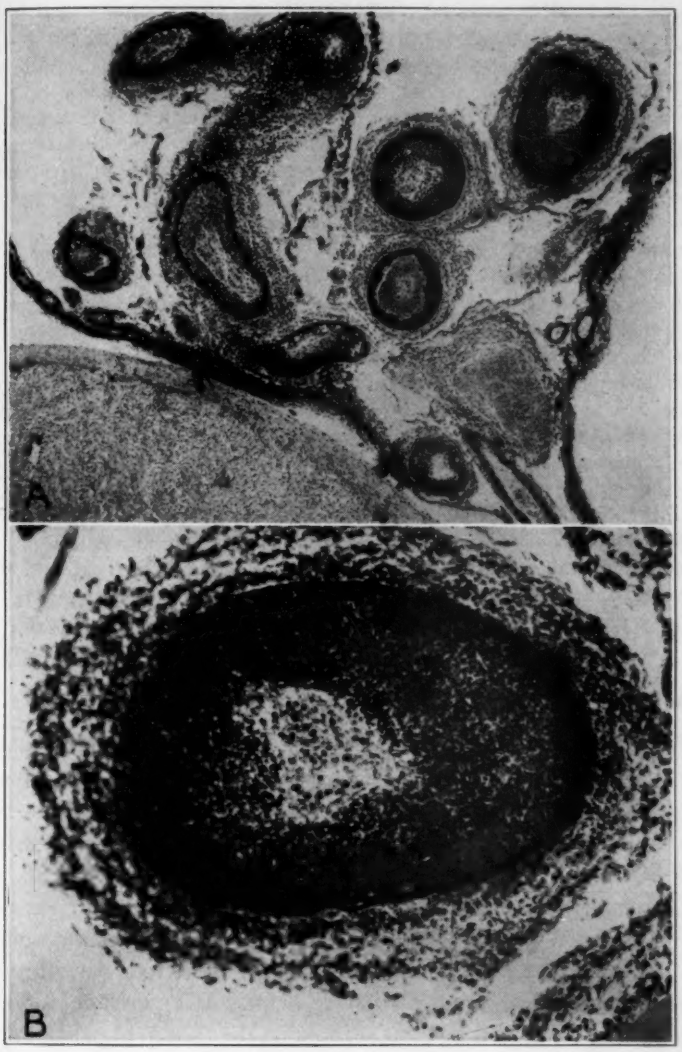

Fig. 10.—*A* (× 46) shows a vascular inflammatory lesion along the ventral surface of the medulla, and *B* (× 200) a necrotic and infiltrated vessel at the base of the medulla. Weigert's elastica stain.

brain stem. The cellular infiltrations seemed to have a direct relation to, in fact, to be secondary to, inflammatory lesions of certain groups of vessels lying in the meninges.

Vessels remote from gross lesions: This inflammatory process was distributed in an irregular fashion, involving groups of vessels, both arteries and veins, along the lateral aspect of both peduncles and adjacent to the lateral geniculate bodies and sparing those in the interpeduncular space. At these points the cellular infiltrations could be followed along the vessels into the inflammatory foci in the midbrain already described. Severe changes were observed in the medium and small arteries and veins along the ventral and lateral aspects of the medulla (fig. 10 *A* and *B*), despite the fact that the medulla itself was practically free from inflammatory lesions. There was considerable variation in the degree and character of the vascular disease. The most severe and striking changes were present in the vessels lying along the lateral and ventral aspects of the medulla. The walls of the vessels were densely infiltrated with lymphocytes and a few polymorphonuclear leukocytes, many of which were undergoing pyknosis. The intima was swollen, staining homogeneous pink in the hematoxylin and eosin sections and homogeneous yellow in the Weigert elastica preparations. There was no intimal proliferation, and although the lumens were somewhat narrowed by the edematous, infiltrated intima, no completely occluded vessels were seen. The internal elastic membrane was preserved in some vessels, while in others it was more or less severely damaged, being thinned, broken and almost completely destroyed in some places. The media in the more severely involved vessels had undergone profound necrosis and, with the adventitia, was densely infiltrated with lymphocytes and polymorphonuclears. The adventitial infiltration was marked, the cells forming collars around the vessels and extending into the adjacent meninges. In the less involved vessels the inflammatory process was limited to the adventitia, leaving the media and intima intact. No nodules or intimal proliferations were seen. An attempt to find the vascular lesions which were probably responsible for the massive necrotizing lesion in the central portions of the brain was unsuccessful. The large vessels at the base and over the convexities showed no evidence of disease.

The cerebellum presented no inflammatory or necrotic foci but a moderate diffuse loss of myelin in the deep medullary substance.

COMMENT

Pathologic-Anatomic Changes.—This case is of unusual interest not only because of the rarity of this type of lesion in the central nervous system but because the condition was diagnosed as cerebral tumor on the basis of clinical study and gross pathologic examination until microscopic sections revealed its true character. Even at operation, a mass lying deep in the brain substance was considered by the neurosurgeon to be neoplastic. Although histologic study of the specimen taken for biopsy revealed only inflammatory changes, they, too, were interpreted as indicating a reactive process in the vicinity of a massive lesion, which was probably neoplastic. On sectioning the brain after fixation, the circumscribed, grayish pink masses occupying the central portions of the brain were thought to be neoplastic. When microscopic sections were observed to consist of peculiar necrotic tissue, it was thought at first that the massive necrosis might represent the central portion of a tumor. Further investigation, however, failed to reveal any neoplastic

tissue, and the peculiar homogeneously pink-staining, structureless material did not present the picture of encephalomalacia caused by ordinary vascular occlusion. The clue to the cause of the massive necrosis was found in the striking inflammatory and degenerative changes in the blood vessels and in the occlusion of many vessels by plugs of fibrin. The impression that the disease might be vascular was borne out by the fact that the vessels remote from the necrotic lesions were also the seat of a severe inflammatory and, in places, a necrotizing process. The disease, therefore, was assumed to be true primary angiitis, as it involved the veins as well as the arteries.

The pathologic picture could not be identified as any of the well known forms of arteritis or angiitis. It was quite different from the syphilitic variety, in that there were no gummatous nodules, no giant cells, no aneurysmal dilatations and no proliferation of the intima, which are common in the syphilitic obliterative endarteritis of Heubner.[2] Moreover, there was no family history of syphilis; the Wassermann reaction of the blood was negative, and Levaditi stains of brain material failed to reveal the presence of spirochetes.

The inflammatory and necrotizing changes in the vessels in this case resembled, to a certain extent, those seen in cases of necrotizing arteritis (periarteritis nodosa). However, the absence of the characteristic changes in the brain makes it inadvisable so to designate this condition, in consideration of the fact that the other organs were not available for study. Grossly the vessels were normal, no nodules or aneurysmal dilatations being present. Kaufmann[2] stated that nodular periarteritis is characterized by multiple, circumscribed, nodular, parietal thickenings in the smaller and even the microscopic arteries of the muscular type. As only about one half of the reports on periarteritis nodosa of the central nervous system[3] have described macroscopic

2. Kaufmann, E.: Pathology for Students and Practitioners, Philadelphia, P. Blakiston's Son & Co., 1929.

3. Literature on periarteritis nodosa involving the central nervous system: (*a*) Chvostek and Weichselbaum: Herdweise syphilitische Endarteritis mit multipler Aneurysmenbildung, Allg. Wien. med. Ztg. **22**:257, 265, 275, 294, 302 and 312, 1877. (*b*) Abramov, S.: Ueber die Veränderungen der Blutgefässe bei der Syphilis, Beitr. z. path. Anat. u. z. allg. Path. **26**: 202, 1899. (*c*) Müller, P.: Ueber Periarteritis nodosa, in Festschrift zur Feier des fünfzigjährigen Bestehens des Stadtkrankenhauses z. Dresden-Friedrichstadt, Dresden, W. Baensch, 1899, p. 457. (*d*) Veszprémi, D., and Janscó, M.: Ueber einen Fall von Periarteritis nodosa, Beitr. z. path. Anat. u. z. allg. Path. **34**:1, 1903. (*e*) Longcope, W. T.: Periarteritis Nodosa, with Report of a Case with Autopsy, Bull. Ayer Clin. Lab. Pennsylvania Hosp., December 1908, no. 5, p. 1. (*f*) Dickson, W. E.: Polyarteritis Acuta and Periarteritis Nodosa, J. Path. & Bact. **12**:31, 1908. (*g*) Pickert-Menke, H.: Ueber einen Fall von Periarteriitis nodosa, Frankfurt. Ztschr. f. Path. **23**:313, 1920. (*h*)

(Footnote continued on next page)

nodules on the vessels of either the brain or the organs of the body or both, the absence of such an observation does not necessarily exclude periarteritis nodosa. Cellular infiltrations, consisting of lymphocytes and, to a less degree, polymorphonuclears, may involve either the adventitia alone or all three coats of the wall, as in the present case. Necrosis is usually most marked in the media, but there is a difference of opinion as to which coat is first affected by the necrotizing process. The picture that is usually present to a greater or less degree, and which was absent in the case under discussion, is proliferation of fibroblasts not only in the media and adventitia, which when localized frequently produces grossly visible nodules, but in the intima. These intimal proliferations and thickenings may be uniform or eccentric, and by bulging into the lumens they are responsible for the characteristic narrowing so commonly described. Runge and Melzer [3p] described a case in which some of the vessels showed marked intimal proliferation with intact media and adventitia. Marked proliferation of fibrous tissue was especially well described by Richardson,[3o] Wohlwill [3j] and Müller [3c] and was mentioned by most of the other writers. The disease process usually involves the smaller arteries. However, the veins are sometimes also affected (Wohlwill [3j]). In the present case the veins and arteries seemed to be about equally involved.

It is possible that more typical lesions of periarteritis nodosa might have been observed in other organs if they had been available for

Manges, M., and Baehr, G.: Periarteritis Nodosa, Am. J. M. Sc. **162**:162, 1921. (*i*) Gerlach, W.: Ueber Periarteriitis nodosa, Klin. Wchnschr. **1**:467, 1922. (*j*) Wohlwill, F.: Ueber die nur microskopisch erkennbare Form der Periarteriitis nodosa, Virchows Arch. f. path. Anat. **246**:377, 1923. (*k*) Lemke, R.: Ein Beitrag zur Frage der Periarteriitis nodosa, ibid. **240**:30, 1923. (*l*) Otani, S.: Zur Frage nach dem Wesen der sogenannten Periarteriitis nodosa, Frankfurt. Ztschr. f. Path. **30**:208, 1924. (*m*) Baló, J.: Ueber eine Häufung von Periarteriitis nodosa Fällen, Virchows Arch. f. path. Anat. **259**:773, 1926. (*n*) Kimmelstiel, P.: Beiträge zur Frage der Periarteriitis nodosa, ibid. **265**:16, 1927. (*o*) Richardson, M.: Läsionen des Zentralnervensystems bei Periarteriitis nodosa, Ztschr. f. d. ges. Neurol. u. Psychiat. **115**:626, 1928. (*p*) Runge, W., and Melzer, R.: Ueber Periarteriitis nodosa mit starker Beteiligung des Zentralnervensystems, J. f. Psychol. u. Neurol. **40**:298, 1930. (*q*) Silbermann, J.: Zur Klinik und pathologischen Histologie der Periarteriitis nodosa, Monatschr. f. Psychiat. u. Neurol. **72**:225, 1929. (*r*) Arkin, A.: A Clinical and Pathological Study of Periarteritis Nodosa, Am. J. Path. **6**:401, 1930. (*s*) Rothstein, J. L., and Welt, S.: Periarteritis Nodosa in Infancy and in Childhood: Report of Two Cases with Necropsy Observations, Am. J. Dis. Child. **45**:1277 (June) 1933. (*t*) Krahulik, L.; Rosenthal, M., and Loughlin, E.: Periarteritis Nodosa (Necrotizing Panarteritis) in Childhood with Meningeal Involvement, Am. J. M. Sc. **190**:308, 1935. (*u*) Urechia, C. I., and Elekes, N.: Les formes nerveuses de l'artérite noueuse de Kussmaul, Ann. de méd. **36**:466, 1934.

study. Although it cannot be stated definitely that this case is not one of periarteritis nodosa, it is considered inadvisable so to classify it, in view of the points already discussed.

Of considerable interest are several communications by Harbitz, of Norway, who in 1922 [4] and again in 1933,[5] under the titles "unknown forms of arteritis" and "arteritis of a peculiar nature," described a number of cases, in several of which the nervous system was involved and the unusual features were of sufficient interest to warrant detailed reproduction.

Case 1 (Harbitz' case 3, 1922 [4]).—A woman aged 26 for two years had had attacks of fainting (during one of which she received a blow on the head), tremors of the hands, double vision and attacks due to vestibular disturbance, with vomiting and convulsive movements of the face. In 1918, one year before admission to the hospital, she had influenza, after which she became worse, with pains in the legs, difficulty in walking and convulsive attacks of a hysterical nature. Examination in March 1919 revealed a dull, rather stuporous, somewhat disoriented woman with monotonous speech, normal eyes and no symptoms on the part of the cranial nerves, pons or bulb. There were reduced strength in the arms, ataxia and paraparesis of both legs, with increased patellar reflexes and a positive Babinski sign. Romberg's sign was present, and there was an uncertain spastic gait. There were no disturbances in sensibility. The patient became bedridden, with increasing stupor, headache, choked disks and increasing paresis of the extremities. The disease was first regarded as multiple sclerosis, but later, as signs of increasing intracranial pressure developed, a tumor of peculiar localization with secondary hydrocephalus was considered. The patient died in May 1919.

Autopsy was limited to the brain. Macroscopically, in the floor of the third ventricle, particularly on the left, were areas of solid, rather tumor-like infiltrations. In the central ganglia were recent areas of hemorrhage, the size of a hen's egg. In the corpus callosum were diffusely infiltrated areas. Microscopically, an inflammatory process in the pia-arachnoid and the brain was closely related to the blood vessels, particularly the arteries, and followed the blood vessels from the pia into the brain substance. The changes were present everywhere, including the base, but were most marked in the central ganglia. The walls of the vessels, especially the arteries, were infiltrated principally with lymphocytes but also with polymorphonuclear leukocytes and plasma cells. Connective tissue cells in the intima and adventitia had proliferated, resulting in a thick ring around the lumens. In the dense infiltrations were many large and small multinucleated giant cells. Many vessels were widened, and there was hemorrhagic infiltration in the brain substance. In many places the process extended throughout the entire segment of the vessel, but in other places the segment was only partially involved. Small arteries were frequently entirely closed, and thrombi

4. Harbitz, F.: Unknown Forms of Arteritis with Special Reference to Their Relation to Syphilitic Arteritis and Periarteritis Nodosa, Am. J. M. Sc. **163**:250, 1922.

5. Harbitz, F.: Cases of Encephalitis Presenting Distinctive Clinical and Anatomical Picture ("Arteritis" of a Peculiar Nature), Acta path. et microbiol. Scandinav., supp. 16, 1933, p. 101.

were present in the lumens. There were no necrotic foci, but in the neighborhood of the severely involved vessels the ganglion cells showed degeneration in varying degree.

In commenting on this case, Harbitz described the condition as a diffuse inflammatory process, the essential lesion being arteritis. The Wassermann reaction was negative. He differentiated the condition from syphilis, on the basis of the negative Wassermann reaction and the absence of gummatous changes and spirochetes, and from encephalitis lethargica and periarteritis nodosa.

Case 2 (Harbitz' case 4, 1922 [4]).—A sailor aged 46, with a history of chancre, suffered clinically from an organic type of psychosis. The condition was apparently periarteritis nodosa or, possibly, syphilitic vascular disease.

Case 3 (Harbitz' case 1, 1933 [5]).—A woman aged 39 had tenderness and proptosis of the right eye and internal and external ophthalmoplegia. The cerebrospinal fluid was normal. The diagnosis was uncertain; involvement of the basal parts of the brain, especially the right frontal lobe, possibly proceeding from a sinus, and a tumor were considered. The patient died without operation. Autopsy revealed thrombosis of the right cavernous and the superficial petrosal sinus and probably the posterior part of the ophthalmic vein. There was no infection in the maxillary or the ethmoid sinuses or in the ears or nose. Section of the right temporal lobe showed a reddish gray, tumor-like infiltration, the size of a Spanish hazelnut, through which ran a thrombosed vein. Grossly this lesion resembled a glioma, with numerous blood vessels. It extended forward toward the right frontal lobe and into the lower outer part of the thalamus. Microscopically there were arteritis and phlebitis, with secondary encephalitis and multiple hemorrhages. The walls of the vessels were necrotic, infiltrated with polynuclears and thrombosed with fibrin. The surrounding brain tissue was infiltrated with leukocytes, and there was necrosis of the parenchyma. The meninges were similarly infiltrated.

Case 4 (Harbitz' case 2, 1933 [5]).—A man aged 46 gave a history for ten years of periodic headaches, which had been localized to the crown since 1931. In 1932 he began to have pain in the left side of the chest and the left arm, hand and thigh. This was followed by a sensation of deadness and numbness in the arm and hand. Memory gradually failed. There was no choked disk; no other physical findings were given. The Wassermann reaction was negative, and the roentgenographic findings were normal. The cerebrospinal fluid was clear. The patient died suddenly. Autopsy revealed that all organs were normal except the brain, which contained several jelly-like masses and grayish yellow nodes scattered throughout the right hemisphere. The right artery of the fossa of Sylvius was thrombosed and possessed roughened sclerotic walls. Microscopically there was arteritis of the artery of the fossa of Sylvius, with multiple secondary necrosis and inflammation in the right cerebral hemisphere. In these areas the vessels were necrotic, infiltrated with polynuclear and mononuclear cells and thrombosed. In some places there were thick, pad-shaped proliferations of intima into the lumens. In other places the muscularis was impaired, and the rest of the wall bulged like a small aneurysm. Areas of encephalomalacia were infiltrated with leukocytes and fat granule cells.

Harbitz considered the condition arteritis of an infectious nature, although no microbes could be observed. He distinguished it sharply from syphilis and rheumatic inflammation of the connective tissue and blood vessels. In his opinion, it corresponded in appearance to what is seen in ordinary infectious inflammation in the various organs.

These cases are of interest not only because of the unusual microscopic lesions but because they possess certain clinical and anatomic features in common with the case under discussion. The "tumor-like infiltration" described by Harbitz in sections of the brain in his first and third cases bear a strong resemblance to the grayish pink masses in the present case, which were thought to be neoplastic on gross examination. That inflammatory granulomatous lesions, such as those in tuberculosis and syphilis, frequently simulate tumor of the brain, both clinically and anatomically, is well known. The microscopic changes described by Harbitz bear considerable resemblance to those observed in the present case. They consisted chiefly of necrosis and inflammatory infiltrations of the walls of the vessels with lymphocytes and polymorphonuclears, narrowing of the lumens, collections of fibrin within the vessels, thrombosis and secondary involvement of the brain substance, producing encephalitis. In his first and fourth cases he also noted proliferation of connective tissue in the intima and adventitia and the presence of multinucleated giant cells, which were not present in the case reported here. Harbitz reported in 1926 [6] an unusual case of arteritis of both carotid arteries with thromboses of their branches, resulting in left hemiparesis, atrophy of the left half of the face, cataract in the right eye, changes in the retinal vessels with demonstrable slowing of the flow of blood and death, due to thrombosis of the left sylvian artery. He observed lymphocytic and plasma cell infiltrations along the vasa vasorum and in the media and adventitia and marked thickening of the intima with narrowing of the lumens. There were no gummas and no giant cells. Harbitz described the lesion as arteritis of unknown source, neither syphilitic nor resembling periarteritis nodosa.

In the present case the pathologic changes in the brain substance divide themselves into two groups, those in the necrotic and those in the non-necrotic areas, both of which were nonspecific and represented the reaction of the nervous system to a noxious agent and to deprivation of blood supply. The profound, coagulating necrosis, however, affecting both mesodermal and ectodermal elements, was somewhat unusual. It is reasonable to assume that the injurious agent, which affected primarily the blood vessels, also produced a direct effect on the brain substance and that the combination of the two factors—obliteration of many blood vessels plus the toxic effects of the noxious agent—resulted in such profound necrosis that only a relatively small number of gitter cells survived around the periphery of the perivascular lacunae. During life, there must have been a considerable proliferative glial reaction, for at the edges of the necrotic areas large gemästete macroglia cells

6. Harbitz, F.: Bilateral Carotid Arteritis, Arch. Path. **1**:499 (April) 1926.

were undergoing clasmatodendrosis. In the non-necrotic parts of the brain the inflammatory process was limited to the vessels, and in these areas a marked glial reaction was evident, consisting of proliferation of astrocytes which showed both progressive and regressive changes, marked increase in glia fibers and an increase and accumulation of oligodendroglia cells along the blood vessels. Proliferation and hypertrophy of microglia cells were noted only in the cortex of the right gyrus cinguli, which was involved in the severe necrotizing process. Except in this one place, the cortex was intact and free from inflammatory changes, but the white matter, especially in the occipital and temporal lobes, showed diffuse demyelinization and diminution in the number of axis-cylinders. These degenerative changes and the proliferative and regressive glial manifestations could have been produced only by the direct action of the etiologic agent, as there was no occlusion of vessels in these areas.

Pathogenic and Etiologic Considerations.—In this case, as in those of Harbitz and in periarteritis nodosa, the pathologic changes indicate what appears to be a primary inflammatory disease of the blood vessels, with secondary manifestations in the brain substance. As in these cases, the pathogenesis and etiology were obscure. The inflammatory process seen in vessels as a result of septic thrombi or of adjacent parenchymatous infection [2] consists of a more localized process, which is quite different from the present picture. In this case one must postulate the presence of a noxious substance of diffuse nature which has affected the cerebral vessels in an extensive, but not a uniform, manner. Whether a similar involvement of the blood vessels of the other organs existed was, unfortunately, impossible to determine. However, no symptoms which might be regarded as indicative of generalized vascular disease or involvement by the disease process of any organs except the brain were noted at any time. What the nature of the injurious substance might be is impossible to determine on morphologic grounds. The absence of demonstrable organisms does not necessarily exclude a bacterial source of the toxin. Arteritis has been described as a complication of numerous acute infections, such as smallpox, scarlet fever, influenza, pneumonia, rheumatic fever, chorea, diphtheria, yellow fever, typhus, typhoid, gonorrheal septicemia and measles.[7] Thayer,[8] in discussing the cardiovascular complications of typhoid, reported the anatomic observations in a case in which acute arteritis of the left middle cerebral artery was present. In typhus, necrosis and infiltration of the walls of the small vessels have been described by

7. Osler, W., and McCrae, T.: Modern Medicine: Its Theory and Practice, ed. 3, Philadelphia, Lea & Febiger, 1927, vol. 4, p. 813.

8. Thayer, W. S.: On the Cardiac and Vascular Complications and Sequels of Typhoid Fever, Bull. Johns Hopkins Hosp. **15**:323, 1904.

Fraenkel.[9] Hassin,[10] in a detailed histologic description of several brains from patients with typhus, observed profound disease of the walls of the vessels without inflammatory changes, which he considered to be due to the typhus virus. Winkelman [11] also reported degenerative changes in the walls of small cortical vessels in cases of severe infection and toxemia.

Worthy of note is the febrile illness which the patient had at the age of 9 years, after which he suffered from frequent colds and "sinus trouble." Although this illness did not have a typical course, scarlet fever, after which inflammatory lesions of vessels occasionally occur, cannot be entirely excluded as a possible etiologic factor, and although no obvious sinusitis was found on physical examination in the hospital, this might also be considered as a possible source of infection. Harbitz [5] suggested that this type of vascular inflammation should be regarded as toxic in origin and the result of sensitization of the connective tissue and blood vessels through bacterial antigens, producing at one or another site local allergic or "hyperallergic" inflammation, representing a kind of anaphylactic phenomenon. Further elaboration of this point is not within the scope of this report, for any conclusions that might be drawn would be based on purely theoretical considerations. Because of the obscurity of the source of the toxic or infectious agent in his cases, Harbitz usually described the condition as arteritis of unknown etiology. As both veins and arteries were extensively involved in the present case, a more accurate and inclusive term would be "necrotizing angiitis of unknown etiology."

Clinical Considerations.—A review of the clinical aspects in this case, with a full knowledge of the anatomic and pathologic lesions, does not, unfortunately, afford any definite information which might prevent a similar diagnostic error in the future. The history of convulsive seizures, mental symptoms, headache and stupor, elevated cerebrospinal fluid pressure and subsequent bradycardia made the diagnosis of an expanding lesion almost compulsory. The ventriculographic studies seemed to corroborate this assumption. The clinical localization of the lesion to the suprasellar region with encroachment on the basal ganglia proved to be approximately, although not completely, correct. Finally,

9. Fraenkel, E.: Ueber Fleckfieber und Roseola, München. med. Wchnschr. **67**:57, 1914.

10. Hassin, G. B.: Brain Changes in Typhus Fever Contrasted with Those in Epidemic Encephalitis and Acute Poliomyelitis, Arch. Neurol. & Psychiat. **11**: 121 (Feb.) 1924.

11. Winkelman, N. W., and Eckel, J. L.: Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929.

the progressive nature of the symptoms and the development of papilledema during the postoperative course appeared to confirm this diagnosis.

Xanthochromia, a high protein content and pleocytosis of the cerebrospinal fluid, although not common, occur occasionally in cases of tumor of the brain, on the surface or near the ventricle. In the present case they were probably due to the extensive ependymitis and low grade meningitic process. Any attempt to correlate with any degree of accuracy the clinical signs and symptoms with the anatomic lesions is practically impossible, because of the widely disseminated distribution of the lesions. The massive involvement of the basal ganglia, the pulvinars, the geniculate bodies and the occipital lobes adequately explains the hyperkinesias and the visual and pupillary disturbances. The extensive changes in both hemispheres must have been responsible for the mental symptoms and convulsive seizures, but it is difficult to understand why these symptoms were present during the earlier course of the disease, when histologically the lesions in the hemispheres appear to be more recent.

It is interesting to compare the clinical picture present in other cases of unusual inflammatory vascular lesions of the central nervous system, as reported in the literature. The rare cerebral forms of thromboangiitis obliterans reviewed recently by Spatz [12] and Albo [13] usually assumed the clinical appearance either of a diffuse cerebral disease, such as multiple or diffuse sclerosis,[12] or of a diffuse or focal vascular lesion.[14] Harbitz' cases of arteritis (cases 1 and 2 in this paper) [15] were considered clinically as instances of probable tumor, and although no diagnosis or physical findings were recorded in the report, the history of headaches and focal symptoms in case 4 would strongly suggest the diagnosis of tumor. A thorough perusal of the literature dealing with cases of periarteritis nodosa involving the central nervous system [3] reveals a diversity of neurologic diagnoses. (In many reports no neuro-

12. Spatz, H.: Ueber die Beteiligung des Gehirns bei der v. Winiwarter-Buergerschen Krankheit (Thrombo-endangiitis obliterans), Deutsche Ztschr. f. Nervenh. **136**:86, 1935.

13. Albo, W. L.: Forma cerebral de la tromboendangiitis obliterans de Winiwarter-Buerger con motivo de una observacion clinica, An. de med. int. **4**:707, 1935.

14. Boyd, W.: The Pathology of Internal Diseases, Philadelphia, Lea & Febiger, 1931, p. 108. Bielschowsky, M.: Cerebrale Veränderungen bei einem Fall von Winiwarter-Bürgerscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **155**:329, 1936. Foerster, O., and Guttman, L.: Cerebral Komplikationen bei Thromboangiitis obliterans, Arch. f. Psychiat. **100**:506, 1933. Essen, K. W.: Hemiplegie bei Endarteriitis obliterans, Deutsche Ztschr. f. Nervenh. **138**:99, 1935.

15. Harbitz, footnotes 4 and 5.

logic diagnosis was given.) If one omits the diagnosis of polyneuritis, which was frequent and does not concern this report, the diagnoses were as follows: encephalitis of the left cerebral peduncle (Chvostek and Weichselbaum [3a]); meningeal or ventricular hemorrhage (Veszprémi and Janscó [3d]); cerebral hemorrhage (Kimmelstiel [3n] and Arkin [3r]); chronic sepsis (Lemke [3k]); chronic alcoholism (Kimmelstiel [3n]); meningitis (Dickson [3f]); (Krahulik and others [3t]); Landry's paralysis (Gerlach [3l]), and disseminated cerebral disease (Richardson,[3o] Runge and Melzer [3p] and Urechia and Elekes [3u]). Tumor was mentioned only twice. In the first instance the diagnosis of sarcomatosis of the meninges (Otani [3l]), however, was not truly that of a focal expanding lesion. The condition in Baló's first case [3m] was considered clinically to be a tumor, but macroscopically the brain showed encephalomalacia and vascular disease.

The preceding brief review discloses as a striking feature the fact that in three of four cases described by Harbitz the condition simulated a tumor of the brain. These cases bore a close resemblance, clinically as well as macroscopically, to the one described in this paper. This was true of only one of the reported cases of periarteritis nodosa. This is particularly significant, since it may be assumed that the symptomatology in cases of this type is more likely to be determined by the anatomic distribution and extent of the lesion than by its character. Thus, it is believed that this form of vascular disease, in spite of its unique character, cannot as yet be fitted into a clinical entity. The clinical manifestations of infection were minimal. Fever was not present terminally in Harbitz' cases, except in case 1. In the present case there was no fever or leukocytosis before operation, but the temperature was slightly elevated during the entire postoperative period. In cases of periarteritis nodosa, however, there is frequently evidence of infection, usually in some other organ, such as the joints, the peripheral nerves or the kidneys, in the presence of which the correct diagnosis can be suspected.

SUMMARY AND CONCLUSIONS

A case is presented of massive necrotizing encephalitis simulating a tumor of the brain, which was due to widespread necrotizing angiitis of unknown etiology. Cases of unusual inflammatory vascular disease of the brain reported in the literature, particularly periarteritis nodosa and the "arteritis" of unknown etiology described by Harbitz, and their relationship to the present case are discussed.

Dr. Joseph H. Globus supervised and advised in the study of this material and the preparation of the report.

WATER METABOLISM IN RELATION TO CONVULSIONS

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The factor of water balance has received much attention from many investigators of epilepsy and the convulsive state. Rowntree [1] produced a condition which he designated as "water intoxication" by administering large amounts of water by stomach tube to various mammals (dog, cat, rabbit, guinea-pig and rat). A prominent feature of this toxic state was the occurrence of convulsions. He regarded such convulsions as the expression of an increase in intracranial pressure arising as a manifestation of disturbance in the salt to water equilibrium of the body and the central nervous system.

The production of convulsions in animals by such forced administration of water suggested a possible disturbance of water balance in epilepsy occurring in man. Temple Fay [2] and his co-workers were impressed by the possible significance of disturbed water balance and stated that "the predisposing factor concerned with a major convulsive seizure is due to a hydration state." McQuarrie,[3] Gamble,[4] Lyon and Dunlop [5] and others likewise supported such a hypothesis. They produced a state of altered water balance in epileptic patients by the administration of pitressin while the intake of water was forced and

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1. Rowntree, L. G.: The Water Balance of the Body, Physiol. Rev. **2**:116, 1922.

2. Fay, Temple: Epilepsy: Clinical Observations on the Control of Convulsive Seizures by Means of Dehydration, J. Nerv. & Ment. Dis. **71**:481, 1930.

3. McQuarrie, I.: Epilepsy in Children: The Relationship of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**:451 (Sept.) 1929.

4. Gamble, J. L.: Dehydration, New England J. Med. **201**:909 (Nov. 7) 1929.

5. Lyon, D. M., and Dunlop, D. M.: Epilepsy and Dehydration, Edinburgh M. J. **40**:266, 1933.

noted an increase in the convulsive attacks. They assumed that a state of positive water balance, or "hydration," was produced by this procedure, as there occurred a fall in urinary output and an increase in body weight, presumably due to storage of water.

More recently, Jacobsen [6] was so convinced of the constancy with which seizures occurred in epileptic children when there was retention of fluid in the body to the degree that a positive water balance resulted, as measured by the preceding criteria, that he proposed a test for epilepsy. In this test fluids are given to the point of establishing a positive water balance, when pitressin (the antidiuretic principle of the posterior lobe of the pituitary) is injected to prevent normal excretion of fluids and thus to cause their supposed retention. Others have used the so-called pitressin test for epilepsy, both in children and in adults, and have confirmed Jacobsen's contentions (Clegg and Thorpe [7]).

Fay [2] utilized the concept of disturbance in water balance in epilepsy as the basis for a plan of therapy. He wrote:

> Proper control of this factor, when possible, gives rise to an attack-free existence which may continue as long as the patient's water metabolism or fluid balance remains within the limits of proper compensation.

He therefore proposed "dehydration"—restriction of fluid intake—as treatment for epilepsy and has reported favorable results from such a regimen. Hartenberg [8] has been credited with having introduced such a procedure as early as 1913.

WATER METABOLISM

Water balance may be defined as the normal relation between the total amount of water entering the organism and the total output from the body by way of the kidneys and other channels.

The total intake of water includes, in addition to water ingested as such, that occurring in other beverages, such as coffee, tea and milk, and in solid foods. To this should be added the water of metabolism resulting from oxidation of organic matter in intracellular respiration and other changes in the molecular structure of substances, such as syntheses concerned in the building up of dextrose into cellulose or starch or of amino-acids into complex proteins. It has been found that in an ordinary diet as much as 1,000 cc. of water a day may be taken

6. Jacobsen, A. W.: Pitressin Test in Epilepsy, New York State J. Med. **34**:506 (June 1) 1934.

7. Clegg, J. L., and Thorpe, F. T.: Induced Water Retention in Diagnosis of Idiopathic Epilepsy, Lancet **1**:1381 (June 15) 1935.

8. Hartenberg, P.: La déshydratation dans le traitement de l'épilepsie, Presse méd. **39**:101 (Jan. 21) 1931.

in the so-called solid foods. This includes the water content of the foods and the water resulting from their oxidation (Rowntree).

The output of water includes much more than that excreted from the kidneys as urine. Peters [9] has called attention to the fact that "the common practice of attempting to estimate water balance by comparing the volume of urine with the various fluids ingested is therefore extremely inaccurate." In addition to the urinary output, considerable water is lost through extrarenal channels, such as in the feces, vaporization from the lungs, evaporation from the skin and radiation and conduction from the skin. Under normal conditions of temperature and humidity approximately 500 cc. of water is lost through the skin as insensible and perceptible sweat during a period of twenty-four hours. Rubner found that in a resting man at 20 C. approximately 400 cc. of water escapes through the respiratory channels. The amount of water in the feces in health is rarely more than 200 cc., and is usually from 60 to 150 cc.

In general the amount of urine excreted is directly dependent on the intake of water and is inversely proportional to the amount of water excreted through other channels (Wiggers [10]). The amount of urine passed in twenty-four hours fluctuates greatly. Ability of the kidney to accommodate itself to fluctuations in the intake of water and of food and to environmental influences constitutes one of its striking characteristics. The average healthy adult passes from 1,000 to 2,000 cc. of urine a day. Even with a constant water intake, the volume of urine is extremely variable for any single day or part of the day. The urinary output is related, among other factors, to the amount of water lost through other channels, to the intake of food and, finally and most important, to that of water. Thus, it is evident that an accurate analysis of water balance must take into consideration the many factors involved in the intake and output of fluid.

In the healthy human subject water taken by mouth is absorbed from the intestine and passes into the blood stream, to be distributed between the plasma and the corpuscles. Some of this fluid passes into the body tissues until an equilibrium in body fluids is reached—the excess being excreted by way of the kidneys or extrarenal channels. The regulation of water balance by the healthy body challenges interference. The changes which occur in composition of the blood after drinking water are small as compared with the enormously increased output of urine.

9. Peters, John P.: Body Water, Springfield, Ill., Charles C. Thomas, Publisher, 1935.

10. Wiggers, Carl J.: Physiology in Health and Disease, Philadelphia, Lea & Febiger, 1934.

FLUID IN THE TISSUES

Water is present in all tissues—within the cells and in the interstitial spaces. Fluid is essential for osmotic adjustments between the tissue cells and their environment. The importance of water in cellular metabolism as the medium for exchange of solutes (electrolytes) is recognized. In general, potassium is confined almost exclusively to the cell, and sodium, to the fluid surrounding the cell; therefore changes in the total exchange of these bases may be interpreted as indicating corresponding movements of the cellular and the interstitial fluid, respectively (Byron [11]).

The fluid composition of tissue cells cannot, like that of blood cells, be determined by direct analysis, because these cells cannot be separated from the interstitial substance which surrounds and connects them. The muscles and liver are the tissues of the body which have been most thoroughly studied as to their water content. In the fresh state they contain from 70 to 80 Gm. of water per hundred grams of tissue.

One of the important functions of the liver is that of storage of water. Any dislocation of water balance is shunted first to the liver and muscles. It is well known that when the liver is injured the blood is diluted. Thus, the liver is an important regulating agent in the partition of water between the blood and the tissues. The quantity of fluid in the interstitial spaces is controlled also by the efficiency of lymphatic drainage. No amount of filtration could increase the volume of interstitial fluid if, as fast as liquid escaped from the capillaries, it was returned via the lymphatics to the blood stream. Heller and Smirk [12] found that there is no regular, appreciable increase in the water content of muscles of the rabbit during normal diuresis, and it is probable that no great storage of water takes place unless the excretion of urine is interfered with, as by administration of a solution of posterior pituitary.

It has been claimed that not all the water in biologic mediums containing proteins and other colloids is available for solvent purposes but that a certain proportion is "bound" by these colloids as "water of hydration" (Peters [9]). The exact nature and behavior of "free" (that is, water which is available for solvent purposes) and "bound" water are still to be determined by study, and this is further evidence of the complexity of the problem of water metabolism.

Attention should be directed also to another rôle of water in the organism referred to as intermediate water exchange. It is known that

11. Byrom, F. B.: Study of Total Exchange of Water, Sodium, Potassium and Nitrogen in Epilepsy, Quart. J. Med. **1**:289, 1932.

12. Heller, H., and Smirk, F. H.: Studies Concerning the Alimentary Absorption of Water and Tissue Hydration in Relation to Diuresis, J. Physiol. **76**:283 (Nov. 5) 1932.

much fluid after absorption from the intestine finds its way back into the alimentary canal as digestive fluids. The total amount of saliva, gastric juice, bile, pancreatic juice and succus entericus entering the intestine far exceeds that of fluid taken by mouth. It has been estimated that the amount of fluid excreted into the intestine daily is from 7,500 to 10,000 cc., or from two to three times that taken by mouth, from three to four times that ordinarily excreted as urine and about twice as much as the total volume of blood (Peters [9]).

HYDRATION

The intake of water is regulated to the needs of the body chiefly through thirst. The amount of water ingested usually exceeds the absolute need, the surplus being excreted readily through the kidneys and extrarenal channels. The elaborate regulating mechanism already referred to maintains a normal water balance. In the healthy animal it is extremely difficult to disturb the regulation of water metabolism. In certain disease states, however, particularly those in which the kidney is damaged, this balance is disturbed, and alteration in water storage results. As a consequence of water retention, edema of tissues occurs, with corresponding clinical features. Experimentally, too, water balance has been altered. Weir, Larson and Rowntree [13] administered large amounts of water to dogs by stomach tube. The quantity of fluid taken in far exceeded the amount which could be removed by the kidneys and extrarenal channels. As a consequence, a condition of "water intoxication" was established, characterized by salivation, twitching, stupor and convulsive seizures. These nervous phenomena were thought to be due to increased production of cerebrospinal fluid and cerebral edema.

As a rule, however, in the healthy animal it is extremely difficult to produce a state of so-called hydration by administration of an excessive amount of fluid, except by such drastic forcing of fluids as was employed by Rowntree. Diuresis and extrarenal excretion succeed a high fluid intake, thus attempting to maintain the balance. Furthermore, any excess of water may be shunted to the liver and muscles, where it may be stored for use when indicated.

As an aid to the production of hydration in animals, Rowntree [1] administered, in addition to large quantities of water, the extract of the posterior lobe of the pituitary gland pitressin, the antidiuretic effect of which theoretically should prevent the development of polyuria under such conditions.

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13. Weir, J. F.; Larson, E. E., and Rowntree, L. G.: Studies in Diabetes Insipidus, Water Balance and Water Intoxication, Arch. Int. Med. **29**:306 (March) 1922.

It has been found that sudden increase in the ingestion of water results in temporary dilution of blood. Heller and Smirk [12] and others observed that in from thirty to sixty minutes after taking from 1 to 1.5 liters of fluid, dilution of the blood occurs, as estimated by the chloride content of the plasma and whole blood, the amount of iron in the whole blood, the percentage of hemoglobin and the protein content of the plasma. Priestley [14] found that in human subjects after administration of large doses of water the dilution of blood as estimated by the hemoglobin content and the dried weight of the blood is slight but that dilution of the electrolytes is readily demonstrated. He attributed these changes to withdrawal of salts from the blood, a natural consequence of storage of water in the tissues.

Heller and Smirk [12] pointed out the fallacy of assuming that an increase in the water content of the blood is evidence that the amount of water ingested is retained in the circulation.

> For example, if a change takes place in the proportion of corpuscles and plasma as a result of splenic contractions, posture or local passive congestion, then since the proportion of solid is greater in corpuscles than in plasma, the percentage water content of a whole blood sample will decrease as the percentage of the volume of corpuscles increases. Again, if for any reason the amount of transudation from the blood into lymph spaces is increased, then the water content of the blood will depend upon the percentage of solids in the transudate which has been lost. In other words, an increase in the water content of the blood, as determined by the percentage of solid residue after drying may merely represent an increase in the proportion of solid residue after a loss of one of the solid constituents of plasma, such as the salt or protein. Moreover, two solutions, each containing 95 cc. of water and in one case 5 per cent of protein and in the other 5 per cent of NaCl are physically and physiologically very different solutions. To give "blood dilution" a precise meaning, it is therefore necessary to state the substance used as an index of dilution and the nature of the diluent.

So long as the rate of absorption of water from the intestine exceeds that of its storage in the tissues, the water content of the blood will continue to increase and dilution of the hemoglobin and protein will be observed. Presumably, as the blood becomes diluted, part of the water taken passes to the tissues.

The mechanisms which keep the blood volume constant under normal conditions and those which increase or decrease it in disease are many and complex. The plasma volume depends to a certain extent on (1) intake and absorption of water, (2) production of water from foods during metabolism, (3) storage and liberation of water by tissues, (4) elimination of water, (5) rate of formation of plasma and (6) loss of electrolytes, as indicated by changes which result from ingestion of

14. Priestley, J. G.: The Regulation of Excretion of Water by the Kidneys, J. Physiol. **50**:304, 1916.

salts, alkalis and acid-producing substances. This loss causes redistribution of water between the blood and the tissues either because electrolytes alter the osmotic pressure of the blood or because they result in shift of ions to the tissues.

The average blood volume of the American or European adult is about 8.8 per cent of the body weight as calculated by the dye method. Of this the plasma volume constitutes from 40 to 60 per cent (Wiggers[10]). Determination of the blood volume as obtained by the dye method may not be an accurate estimation of the total blood volume of the body. The amount of blood pumped through the body at a given time is regulated by the needs of the body. One must distinguish between the volume of blood in the general circulation and the total volume. A large portion of the total volume of blood can be kept out of circulation temporarily, primarily in the portal system, and the dye therefore does not enter this portion. Hence, the dye method determines the volume of blood in the general circulation and not the total volume and may show no increase when a large amount of water is ingested, even with an antidiuretic (Crandall[15]).

Water in the tissues is related directly to the concentration of electrolytes. Regulation of tissue fluid in the healthy body, as well as water balance, challenges interference. The body fluid perhaps is estimated most commonly at present by the thiocyanate method of Crandall and Anderson.[16] The available fluid in man, as calculated by this method, is from 21.2 to 26.4 per cent of the body weight. In states of superhydration and dehydration alterations in the amounts of body fluid may be demonstrated. There are many technical difficulties, however, and the resulting measurements of the total water content of the body may be inexact.

The relationship between the body fluid of the blood and tissues and the urinary output is of interest. It has been found that the rate of formation of urine is not proportional to any extra water present in the blood and tissues at a given moment. Furthermore, it was shown by Heller and Smirk that diuresis following ingestion of water may take place when the water reserves are depleted. This fact has been of practical value in the treatment of mine workers, who are subjected to conditions producing body dehydration, by administration of salt water. Pure water ingested passes through the body and is eliminated through diuresis without being taken up by the depleted tissues. The

15. Crandall, L. A.: Personal communication to the authors.

16. Crandall, L. A., and Anderson, M. X.: Estimation on the State of Hydration of the Body by the Amount of Water Available for the Solution of Sodium Thiocyanate, Am. J. Digest. Dis. & Nutrition **1**:126, 1934.

addition of an electrolyte (sodium chloride), however, creates a new relationship between water and electrolytes, whereby fluid is retained in the tissues.

The antidiuretic action of a solution of posterior pituitary was attributed by Fremont-Smith and his associates [17] to its vasoconstrictor properties, thus interfering with elimination through the kidneys. It was thought that, since the water given is not excreted, practically all the water must be distributed between the blood and the tissues, so that if one estimates the increased amount of water in the blood one will be able to determine the approximate amount that must be stored in the tissues. Byrom,[11] however, found that a solution of posterior pituitary, while postponing the excretion of water, does not hinder the elimination of electrolytes. Consequently, unless the extra fluid administered contains salt, a solution of posterior pituitary will cause not only an increase in the amount of body fluids but a dilution of the tissue fluids. McQuarrie,[3] furthermore, found that when a saline solution is substituted for water and is given in large quantities no convulsions follow, although the extra fluid is retained. This implied that the convulsions arising from administration of pitressin and large amounts of fluid are referable not to actual change in the bulk of body fluid but to a secondary derangement in the balance of water and electrolytes.

RELATION OF BODY FLUID AND EPILEPSY

A possible relationship between disturbance of body fluids and epilepsy has been emphasized by Fay, Gamble, McQuarrie and others. Supposed artificial alterations in water balance have been found to modify the incidence of epileptic seizures. As Byrom pointed out, however, it does not follow that the convulsions in epilepsy are caused by disturbance of water balance, analogous to the convulsions which Weir, Larson and Rowntree induced in animals by forced administration of water. Gamble and Hamilton [18] reported that in epileptic children excretion of sodium rose considerably during periods of convulsions, and they interpreted this change as indicating loss of extracellular water during the convulsion. They were unable to decide whether or not the loss was simply a result of the seizure. Gamble [4] maintained that the epileptic person stores water between attacks, which is released immediately after the seizure. He stressed the concept that apparently there is an underlying disturbance in the control of body fluid in epilepsy.

17. Fremont-Smith, F., and others: Studies in Edema: I. The Mechanism of Water Diuresis in Man, J. Clin. Investigation **9**:7, 1930.

18. Gamble, J. L., and Hamilton, B.: The Acid-Base Composition of Urine from an Epileptic Child, Bull. Johns Hopkins Hosp. **41**:389, 1927.

Later, Hodskins and his collaborators [19] reported that a trend toward higher values for blood volume was found in seventy-eight patients with epilepsy, as compared with the findings for forty-two subjects used as controls. Lennox and Cobb [20] reported normal values for blood cells as estimated by the hematocrit in one hundred patients with epilepsy. They did not, however, state the time of examination of the blood in relation to the occurrence of convulsions. Brown [21] reported normal blood viscosity (4.8) in epileptic patients. Brühl [22] found that the amount of chloride in the blood was within normal limits. Occasionally persons showed an increase after a seizure. The amounts of nonprotein nitrogen and creatinine in the blood of the epileptic person, as studied by Lennox, O'Conner and Wright,[23] showed no significant deviation from the normal. Fletcher and Pedan [24] investigated the blood chemistry of epileptic patients at a quiescent period and during a convulsion. They reported no significant difference in the composition of the blood, except possibly a greater variation in the percentage volume of red cells and a slight rise in serum calcium during the convulsion. They concluded that the changes were not marked enough or sufficiently constant to lend support to the view that onset of an epileptic seizure is associated with alteration in water metabolism. It may be seen that little evidence has been offered to support the notion that in the epileptic patient there is a state of abnormal water metabolism.

Attempts have been made to modify the water balance of the epileptic patient by forcing fluids to the point of producing a state of supposed water retention. McQuarrie [3] attempted to create a state of hydration in epileptic patients by supplementing forced intake of fluid with injections of a solution of posterior pituitary. He reported an increase in weight which, because of diminished urinary output, was assumed to be due to storage of water. There is no proof, however, that a state of hydration was produced by such a procedure. The cerebrospinal fluid pressure was not increased during this period of so-called hydration. Jacobsen [6] gave young epileptic patients 300 cc. of water every two hours

19. Hodskins, M. B.; Guthrie, R. H., and Naurison, J. Z.: Studies in Blood Volumes of Epileptics, Am. J. Psychiat. **11**:623, 1931.

20. Lennox, W. G., and Cobb, S.: Epilepsy, from the Standpoint of Physiology and Treatment, Medicine **7**:105, 1928.

21. Brown, R. D.: The Viscosity of the Blood in Epilepsy, J. Ment. Sc. **56**:686, 1910.

22. Brühl, F.: Weitere blutchemische Untersuchungen zur Pathologie des epileptischen Krampfanfalles, Ztschr. f. d. ges. Neurol. u. Psychiat. **84**:642, 1923.

23. Lennox, W. G.; O'Conner, M., and Wright, L. H.: Studies of the Metabolism in Epilepsy: I. Nonprotein Nitrogenous Constituents of Blood, Arch. Neurol. & Psychiat. **11**:54 (Jan.) 1924.

24. Fletcher, R. T., and Pedan, O. D.: Blood Chemistry in Epilepsy, Lancet **1**:1382 (June 15) 1935.

for ten doses, at the same time injecting graduated doses of pitressin every four hours. He interpreted the increase in body weight as an indication of hydration, stating that an increase in body weight of from 3 to 6 per cent is evidence of a positive water balance. In some instances he could not produce an increase in body weight in spite of the injection of pitressin. Although other investigators have obtained in many instances a rise in body weight after forced feeding of fluids combined with injection of pitressin, they have not adduced clearcut evidence of a state of hydration. It will be seen later in our study that changes in body weight were not constant and could not be accepted as evidence of a state of positive water balance. Clegg and Thorpe [7] produced convulsions in twelve of sixteen epileptic patients in whom they attempted to induce water retention by this method. They mentioned an increase in body weight in one case. They attempted to demonstrate a state of hydration by determining the freezing point of the blood serum. In three cases they found lowering of the freezing point, implying dilution of the blood. In most instances, however, there was no evidence to support the contention that a state of hydration had been produced.

According to Fay,[2] limiting the intake prevents this assumed state of water retention and diminishes or stops convulsive seizures. He termed this regimen "dehydration." By limiting the fluid intake the water reserves of the body are called on, and eventually, as a result of elimination of the fixed base, a state of acidosis is produced, loss of the fixed base being accompanied by parallel withdrawal of water from the body. It is claimed that other procedures, such as fasting and the administration of a ketogenic diet, produce analogous dehydration of the tissues and resulting acidosis. The effects of deprivation of water on dogs was studied by Keith,[25] who reported a decrease in the amount of circulating blood, on the basis of estimations of the blood and plasma. Associated with the diminished blood volume there was increased viscosity of the whole blood. Most investigators have agreed, however, that it is difficult to produce a state of dehydration, even in the experimental animal. Metabolic water produced by cellular oxidation, etc., tends to prevent disturbance of the water balance to the negative side. On the whole, however, loss of body weight and increase in concentration of the blood may be shown to result from limitation of fluid intake. That such a state prevents the occurrence of convulsions is controversial. Cameron [26] studied twelve deteriorated epileptic patients with dehydration and found no definite decrease in the incidence of convulsions, but, on the other hand, an increase.

25. Keith, N. M.: Blood Volume Changes Following Water Abstinence, Am. J. Physiol. **59**:452, 1922.

26. Cameron, D. E.: Dehydration Method in Epilepsy, Am. J. Psychiat. **11**: 123, 1931.

Fetterman and Kumin [27] treated twenty-one patients with epilepsy, sixteen of whom had seizures of the idiopathic, four of the organic and one of the hysterical type. They stated that dehydration produced no clearcut instance of marked improvement in the number of attacks and that change to hydration did not precipitate attacks of convulsions with any regularity. Wilson and Limberger [28] also studied twenty-three epileptic patients with dehydration and hydration. They concluded that dehydration may be of service in the treatment of some epileptic patients if combined with other accepted forms of therapy, but that by itself it is not of much value. They also stated that large amounts of fluid do not increase the number of convulsions. Stubbe Teglbjærg,[29] in a detailed monograph on epilepsy and water metabolism, stated that epileptic seizures do not appear to be accompanied by gross changes in the water balance of the organism. He stated that the pressure theory of Fay is not correct, for superhydration never causes an increase in intracranial pressure like that which follows the Queckenstedt test or a vigorous cough. He claimed that the idea that changes in local pressure in the brain cause epileptic convulsions is unfounded. He observed no constant relation between the seizures and the phases in which he saw universal retention of water. Teglbjærg sought an explanation of the connection between epilepsy and water metabolism in focal cellular conditions in the central nervous system. Ziskind and Bolton [30] studied thirty-one epileptic patients with superhydration, who were given 7 quarts (7.7 liters) of water at the rate of 1 quart (1.1 liters) every thirty minutes, and produced a convulsion in only four cases.

PRESENT STUDY

In this study eighteen young adult patients with recurrent convulsions were hospitalized. All medication was stopped one week before the patient entered the hospital. The investigation was conducted so as to study the patients during each of three periods designated: those of control, hydration and dehydration, respectively.

During the first two or three days the patients were given a normal diet and were permitted fluids according to their usual habits. This period served as the control. An accurate account of the total fluid intake and the urine output was kept during a period of twenty-four hours, designated from 6 a. m. to 6. a. m. on the following day. Studies of the blood during this period included hematocrit determinations and estimations of the blood volume, plasma volume, total amount

27. Fetterman, J. L., and Kumin, H. J.: Dehydration in Epilepsy, J. A. M. A. **100**:1005 (April 1) 1933.

28. Wilson, G., and Limberger, W. A.: Use of Dehydration in Epilepsy, J. A. M. A. **101**:110 (July 8) 1933.

29. Stubbe Teglbjærg, H. P.: Investigations on Epilepsy and Water Metabolism, Acta psychiat. et neurol., supp. 9, 1936, p. 1.

30. Ziskind, E., and Bolton, R.: Insulin Hypoglycemia in Epilepsy, Arch. Neurol. & Psychiat. **36**:331 (Aug.) 1936.

of protein and halide (chloride) content of the blood and body fluid. Patients were weighed twice daily (at 6 a. m. and 6 p. m.). A careful account of all seizures was kept. Data on eighteen epileptic patients were obtained during this period.

After this study made as a control, the fluid intake was increased with the view to obtaining a state of hydration. To one group of seven patients 400 cc. of water was given every two hours. Jacobsen gave 300 cc. every two hours; his patients were children, however. Consequently, in this study on adults it was thought advisable to give a larger amount. In addition to the program of forced water intake, pitressin was given every four hours—starting with 0.2 cc. and increasing to 0.3 and 0.4 cc. and thereafter to 0.5 cc. until ten doses had been given by subcutaneous injection. The diet during this period contained a high fluid content, calculated to be approximately 2,200 cc. per ration for twenty-four hours. Other patients were treated differently. In some subjects as high as 10,000 cc. of fluids per twenty-four hours was given—certain of these patients receiving daily in addition one large dose of pitressin (1.0 cc.) during the period of so-called hydration. In all instances the period of high fluid intake lasted two or more days. Determinations of blood chemistry studies on body fluid and daily records of weight were obtained, as in the control period, and the occurrence of seizures was carefully noted.

After this period of "hydration," the fluid intake was restricted for the purpose of producing a state of dehydration. In most instances no water was permitted as beverage, the only fluid consumed being that in the diet, which totaled as a rule not more than 1,000 cc. per twenty-four hours. Studies of the blood, records of weight and observations of all seizures were made during this period.

RESULTS FOR PERIOD USED AS CONTROL

In eighteen epileptic patients the following facts were noted: The ratios of fluid intake and fluid output did not differ from accepted normal variations. Hematocrit values varied from 38 to 50 per cent, which were well within the range of normal. The blood volume in most instances was found to be in agreement with the upper limits of normal (from 7.5 to 10 per cent of body weight). Hodskins and his co-workers[19] have called attention to this trend toward higher values for blood volume in epileptic persons. It may be seen in the table, however, that in several instances in which more than one determination was obtained during this period a wide variation occurred. Attention has already been called to the fact that in the dye method for determination of blood volume there are many opportunities for error.

The figures for body fluid as obtained by the thiocyanate method of Crandall and Anderson[16] also showed a tendency to be at the high level of, or slightly above, normal. Again, it must be admitted that more data are necessary regarding variations in the normal and the avoidance of errors in the test procedure before one can arrive at a definite conclusion as to the exact nature of this factor in the epileptic patient.

Determinations of the protein and chloride contents of the blood were found to be well within the limits of normal. Five of the eighteen patients had convulsions during the control period. Two patients had one seizure, one patient had two attacks, one four and one five (table 1).

TABLE 1.—*Data on Eighteen Epileptic Patients During a Period of Control*

Patient	Date	Water Intake by Mouth, Cc.	Total Fluid* Intake, Cc.	Output of Urine, Cc.†	Specific Gravity of Urine	Body Weight		Blood Volume		Body Fluid		Hematocrit Readings, %	Blood Plasma, Cc. per Kg.	Blood Protein, %	Blood Halides (Chlorides), Mg.	No. of Fits
						Lb.	Kg.	Cc. per Kg.	% Body Weight	Liters	% Body Weight					
F. G.	9/ 6	1,800	3,460	1,250	1.014	127.5	58	80	12.5	12.5	22	48	41.4	7.29	Not determined	None
	9/ 7	1,800	3,405	2,450	1.012					13	21					
C. S.	9/ 5	1,600	2,955	1,350	1.004	135	61.5	83.5	11.9	19	31	46.5	50.5	7.5	Not determined	None
	9/ 6	1,800	3,400	1,735	1.008											
P. L.	9/19	2,350	3,750	1,850	1.013	129.25	58.5	100.5	9.95	18.8	32	46	54	7.5	Not determined	None
	9/20	3,800	5,200	2,200	1.006											
J. R.	9/ 5	3,100	4,655	3,750	1.007	165	75	88.5	11.8	18	24	44	49.5	7.68	Not determined	None
	9/ 6	2,000	3,660	1,610	1.007											
J. G.	9/17	2,100	3,500	1,350	1.025	133.5	61	83.5	11.9	20	33	47	43.5	8.1	Not determined	2
								111	9	33	54	48	55.5	6.2		
C. H.	9/17	2,300	4,380	1,025	1.011	135	62	91	10.9	16	26	50	45.5	6.7	Not determined	1
	9/18	3,600	5,300	2,610	1.000			85	11.7	23	37	40	51.0	6.25		
R. J.	11/26	1,400	2,800	1,950	1.016	116	52.7	90	11	15.5	29	47.8	47	6.9	495	1
	11/27	1,400	2,800	950	1.018			75.8	13.1	17.5	33.4	42.6	43.5	7.0	520	
	11/28	1,700	3,100	1,350	1.015											
I. F.	11/27	500	1,900	500	1.015	98	44.6	103	9.7	12.8	28	38.7	66	8.0	520	4
	11/28	600	2,000	1,350	1.018	96	43.6	112	8.9	15.6	25.7	43.2	63.5	8.0	514	
D. L.	12/ 6	1,100	2,500	1,500	1.018	108.5	49.3	58.2	17.3	17.5	35.6	42.3	33.6	7.25	480	None
	12/ 7	950	2,350	800	1.018	108	49	102.3	8.7	17	34.5	43	58.3	7.0	500	
M. L.	12/13	1,040	2,440	1,380	1.022	116	52.7	91.8	10.8	17	32.3	46.7	48.9	7.9	510	None
	12/14	700	2,100	1,360	1.020	116.25	52.8	91.8	10.8	21.8	41	41.2	54	7.3	520	
M. D.	12/13	920	2,320	625	1.022	98.75	44.8	89.7	11.1	15.8	39.4	44.3	50.1	7.6	470	5
	12/14	840	2,240	310	1.025	101.25	46	110	9			40.2	73.7	7.2	470	
E. S.	11/30	1,200	2,600	2,450	1.015	115	52.2	98.7	10.1	12.4	23.7	41.8	57.5	7.0	510	None
	12/ 1	2,750	4,150	3,150	1.018	115	52.2	101	9.9	16.1	30.8	45.4	55.1	7.1	500	
V. S.	12/17	1,270	2,670	1,120	1.015	128.25	58.2	86.8	11.5	14.8	....	44.9	47.8	7.6	483	None
	12/18	1,350	2,750	650	1.018	126.25	57.4	86.2	11.6	17.7		42.4	49.7	7.3	480	
R. R.	9/16	1,600	3,000	1,460	1.022	145.2	66	111	9	16	24	43	63.5	7.81	Not determined	None
M. H.	9/26	2,650	3,710	2,850	1.005	82	40.8	80.5	12.4	14.5	36.4	41	47	7.2	Not determined	None
G. K.	9/26	2,700	3,745	2,600	Not determined	113.9	51.8	99	10.1	16.5	29.5	36	63.5	6.01	Not determined	None
D. G.	9/26	2,700	3,855	2,650	1.004	125.4	57	75	13.3	18	31.6	37	47.5	6.33	Not determined	None
A. D.	9/22	4,300	6,040	1,500	1.010	156.5	71	85	11.7	17	24	49	44	6.9	Not determined	None

* This amount includes water and the fluid present in beverages and food.
† To this amount should be added the average daily output of approximately 1,000 cc. by extrarenal channels, such as respiration, feces and sweat.

RESULTS OF PERIOD OF HYDRATION

The data on thirteen patients under a regimen of forced intake of fluid may be listed as follows: The ratios of fluid intake and fluid output in most instances showed preponderance of fluid intake, implying that not all the water ingested was excreted and, hence, supporting the general assumption that a state of water retention, or "hydration," had been achieved. That this conclusion is extremely inaccurate, however, has already been indicated. Nevertheless, the data obtained will be summarized and criticized.

It may be seen that, in spite of the administration of pitressin, polyuria was produced, with the production of urine of very low specific gravities. The curves for changes in body weight show that in seven patients there was a rise, whereas in six there was a fall. The distribution of loss and of increase in weight was unaffected by the method of hydration. According to the contention of other investigators that gain in body weight is an index of the production of a state of hydration, almost half of the patients were not hydrated. It might be noted that the records for body weight showed individual fluctuations during a period of twenty-four hours and were influenced by many factors. Theoretically, the recording of body weights, a comparatively simple technic, should give reliable findings. That difficulties of interpretation may arise, however, is obvious.

The inconstancy of figures for blood volume and body fluid for this period of high water intake precludes any critical deductions. A slight fall in hematocrit values occurred in most cases. This may be interpreted to support the idea that dilution of the blood occurred. The differences between these values and those obtained during the period of control, however, are not in excess of the normal deviation and, hence, cannot be given particular significance. Values for blood plasma showed no significant changes during this period. Values for the protein and halide contents of the blood likewise remained within normal limits—in some cases much higher and in others much lower than those in the control period. Five of the thirteen patients had convulsions during this period of high fluid intake. Of this group only one patient had a seizure during the period of "hydration" and not during that of control or of dehydration. Thus, the incidence of convulsions occurring in this series of patients is not increased with the so-called hydration regimen (table 2).

RESULTS OF PERIOD OF DEHYDRATION

Data were obtained on twelve patients of this group during a period of restricted fluid intake, or dehydration. The records for fluid intake and fluid output suggest depletion of fluids. The specific gravity of urine excreted was in every instance much higher than that in the period used

TABLE 2.—*Data on Thirteen Epileptic Patients During Period of Hydration*

Patient	Date	Water Intake by Mouth, Cc.	Total Fluid Intake, Cc.	Output of Urine, Cc.	Specific Gravity of Urine	Body Weight		Blood Volume		Body Fluid		Hematocrit Readings, %	Blood Plasma, Cc. per Kg.	Blood Protein, %	Blood Halides (Chlorides), Mg.	No. of Fits
						Lb.	Kg.	Cc. per Kg.	% Body Weight	Liters	% Body Weight					
F. G.	9/ 8	6,700	8,705	5,700	1.000	130.5	59.5	95.0	10.5	13.0	21.0	42.5	53.0	6.7	Not determined	None
	9/ 9	5,400	7,445	7,525	1.001											
C. S.	9/ 8	6,700	8,705	3,650	1.001	135.25	61.5	99.0	10.1	17.0	28.0	40.0	59.0	6.5	Not determined	None
	9/ 9	5,600	7,645	2,825	1.000											
P. L.	9/21	8,200	9,570	6,400	1.004	129	58.3	Not satisfactory		Not satisfactory		44.0	Not satisfactory	7.2	Not determined	1
	9/22	5,000	6,795	4,250	1.000											
J. R.	9/ 8	6,800	8,905	5,250	1.002	160	73	86.0	11.6	17.0	24.0	38.0	53.5	7.33	Not determined	None
	9/ 9	6,300	8,345	5,250	1.003											
J. G.	9/18	5,600	7,520	5,150	1.002	132.75	61	93.0	10.7	26.0	41.0	46.0	50.0	7.2	Not determined	1
	9/19	5,600	7,195	3,570	1.004											
C. H.	9/20	9,000	10,180	2,512	1.007	135	61	99.0	10.1	20.4	33.0	48.0	51.5	6.7	Not determined	None
	9/21	5,000	6,700	5,100	1.007											
R. J.	12/ 3	1,900	3,300	2,850	1.010	114.75	52.1	97.1	10.2	14.8	28.1	44.9	53.5	7.3	524	None
	12/ 4	2,600	4,000	1,850	1.010			95.1	10.5	15.0	29.0	44.2	53.1	7.6	505	
I. F.	12/ 1	2,750	4,950	2,500	1.008	97.5	44.3	112.0	8.9	16.6	37.5	37.3	70.6	7.4	538	None
	12/ 2	2,700	4,900	2,100	1.010											
D. L.	12/12	3,418	5,618	2,030	1.025	108	49.09	98.0	10.2	17.7	36.1	40.5	58.7	7.3	514	None
	12/13	3,200	5,400	1,430	1.015											
M. L.	12/19	2,700	4,900	2,550	1.015	116.25	52.8	92.5	10.8	19.4	36.4	41.6	54.0	7.6	455	None
	12/20	3,750	5,950	1,850	1.008											
M. D.	12/20	3,020	5,250	2,575	1.010	101.5	46.1	92.8	10.7	16.2	35.5	40.5	55.2	7.3	490	3
	12/21	3,775	5,975	2,500	1.002											
E. S.	12/ 4	2,400	4,600	3,100	1.010	114	51.8	91.3	10.9	18.3	35.3	41.6	53.3	7.3	500	3
	12/ 5	2,400	4,600	2,310	1.010											
V. S.	12/20	3,400	5,600	700	1.010	126	57.2	75.9	13.1	16.8	29.3	49.5	38.2	8.0	505	1
	12/21	3,820	6,020	2,050	1.006											

TABLE 3.—*Data on Twelve Epileptic Patients During Period of Dehydration*

Patient	Date	Water Intake by Mouth, Cc.	Total Fluid Intake, Cc.	Output of Urine, Cc.	Specific Gravity of Urine	Body Weight		Blood Volume		Body Fluid		Hematocrit Readings, %	Blood Plasma, Cc. per Kg.	Blood Protein, %	Blood Halides (Chlorides), Mg.	No. of Fits
						Lb.	Kg.	Cc. per Kg.	% Body Weight	Liters	% Body Weight					
F. G.	9/11	0	1,553	1,380	1.012	128.25	58	94	10.6	19.5	34	47	50	7.0	Not determined	None
	9/12	0	1,285	900	1.019			77.5	12.7	19.6	32.4	45	43	7.3		
C. S.	9/11	0	1,555	460	1.008	135	61.5	112	8.9	17	26	46	60.5	6.9	Not determined	None
	9/12	0	1,230	820	1.024			57.6	17.3	16.7	27	45	31.8	7.44		
P. L.	9/23	0	795	780	1.020	129.25	58.5	184	5.4	16	27	47	81.5	7.81	Not determined	1
	9/24	0	855	1,390	1.018											
J. R.	9/11	0	1,555	850	1.009	158	72	95	10.5	23	32	42	55	7.44	Not determined	1
	9/12	0	1,285	810	1.014	161	73	35	28.5	21.8	30	41	20.5	7.68		
J. G.	9/21	0	595	575	1.025	129	58.5	104	9.6	23	39.4	51	51	6.25	Not determined	1
	9/22	0	675	760	1.018											
C. H.	9/22	0	510	575	1.012	Not determined		Not determined		Not determined		Not determined	Not determined	Not determined	Not determined	None
	9/23	25	1,025	Not determined												
R. J.	12/ 7	0	1,000	450	1.032	112	50.9	82.3	12.1	16.6	33	45.6	44.8	7.6	490	None
	12/ 8	0	1,000	600	1.038											
I. F.	12/ 5	0	1,000	325	1.022	92	41.8	82.5	12.1	15.6	57.3	43.4	46.7	7.9	505	3
	12/ 6	0	1,000	700	1.030											
D. L.	12/15	0	1,000	700	1.030	104	47.2	97.5	10.2	11.12	23.5	43.1	55.2	7.6	488	None
	12/16	0	1,000	1,030	1.030											
M. L.	12/22	0	1,000	165	1.035	108.5	49.3	94.2	10.6	12.1	32.3	41.9	59.9	7.6	480	None
	12/23	0	1,000	400	1.030											
M. D.	12/24	200	1,200	No record	1.019	Not determined		Not determined		Not determined		Not determined	Not determined	Not determined	Not determined	None
	12/25	400	1,400	No record	1.019											
E. S.	12/ 8	0	1,000	950	1.015	109.5	49.7	77	12.9	16.2	32.3	39	47.9	7.6	528	2
	12/ 9	0	1,000	700	1.015											

as a control. In most cases a drop in blood volume was obtained. In several instances, however, this drop was so marked that the accuracy of the technic and possibly the reliability of the method were questioned. This has been commented on previously. Findings for body fluid in general showed a drop to support the depletion of water storage. In a few instances a rise was recorded. Furthermore, the drop in body

TABLE 4.—*Correlation with*

Name	No. of Fits	Time	Data Obtained		Body Weight, Lb.		Hematocrit Readings, %	
			Before	After	Before	After	Before	After
J. R.	1	11/27/35 3:30 p.m.	24 hr.	48 hr.	116	115	47.8	42.6
E. S.	4	11/27/35 2:30 p.m. 9:00 p.m. 11/ 8/35 2:35 a.m. 6:20 a.m.	28 hr. before first seizure	76 hr. after last seizure	114	109½	41.6	39
P. L.	2	9/21/35 7:20 a.m. 9/25/35 5:00 a.m.	42 hr. before first seizure	49 hr. after first seizure	129¼	129¼	46	47
I. F.	4	11/26/35 2:00 a.m. 11/27/35 4:00 a.m. 12 midnight 12/ 4/35 4:30 a.m.	13 hr. before last seizure	108 hr. after last seizure	96	92	37.3	43.4
C. H.	1	9/20/35 8:00 a.m.	41 hr.	29 hr.	135	135	40	48
J. G.	5	9/17/35 9:00 p.m. 9/18/35 2:57 a.m. 12:30 p.m. 7:30 p.m. 9/23/35 7:45 a.m.	(a) 7½ hr. before first seizure	(b) 42½ hr. after fourth attack (c) 25 hr. after last seizure	(a) 133½	(b) 132¾ (c) 129	(a) 47	(b) 46 (c) 57
J. R.	1	9/13/35 6:30 p.m., after dehydration	100 hr.	64 hr.	160	161	38	41
V. S.	1	12/20/35 12 noon	20½ hr.	50½ hr.	126¼	126	42.4	49.5
M. D.	9	12/15/35 9:30 a.m. 12 midnight 1:18 p.m. 2:00 p.m. 6:35 p.m. 12/19/35 8:15 p.m. 12/20/35 8:00 a.m. 12 noon 12/24/35 12 noon	(a) 47 hr. before first seizure	(b) ½ hr. before and after third fit (c) 5½ hr. after fifth fit (d) 46½ hr. after eighth fit	(a) 98	(b) 98¾ (c) 101¼ (d) 100½	(a) 40.9	(b) 44.3 (c) 40.2 (d) 40.5

fluid recorded in several cases was so large as to throw doubt on the reliability of the determinations. A slight rise in the cell volume and the protein content of the blood was recorded in most instances, but the degree of the increase was too slight to be considered significant. The halide content of the blood rose in three cases, fell in four and remained unchanged in one. A fall in body weight occurred in every instance. That this change indicates a state of "dehydration," however, is hardly an accurate conclusion, unless it is substantiated by other evidence of loss of body fluid, blood volume, etc.

Five patients in this group had one or more convulsions. Two of these had seizures during "hydration." One patient had one or more convulsions in each of the three periods. One patient had no seizure during the control period and none until the end of the period of "hydration," after the last dose of pitressin had been given and limitation of fluids was begun. At that time she had three convulsions, and the following day, while on the dehydration regimen, two more. Thus, it may be seen in our study that in an acute experiment restricting the fluid intake does not prevent the occurrence of seizures. Furthermore, we did not obtain conclusive evidence that a state of dehydration can be produced by such a procedure (table 3).

Occurrence of Seizure

Blood Volume, Cc. per Kilogram		Plasma Volume, Cc. per Kilogram		Blood Protein, %		Blood Halides, Mg.		Body Fluid, Liters	
Before	After	Before	After	Before	After	Before	After	Before	After
90.0	75.8	47	43.5	6.9	7.0	495	520	15.5	17.5
91.3	77.0	53.3	47.9	7.3	7.6	500	528	18.3	16.0
100 5	184.0	54	81.5	7.5	7.81	...	...	18.8	16.0
112.0	82.5	70.6	46.7	7.4	7.9	538	505	16.6	15.6
85.0	90.0	51	5.5	6.25	6.7	...	...	23.0	20.4
(a) 83.5	(b) 93.0	(a) 43.5	(b) 50	(a) 8.1	(b) 7.2	...	...	(a) 20.0	(b) 26.0
	(c) 104.0		(c) 51		(c) 6.25				(c) 23.0
86.0	35.0	53.5	20.5	7.3	7.68	...	...	17.0	21.8
86.2	75.9	49.7	38.2	7.3	8.0	480	505	17.7	16.8
(a) 88.6	(b) 89.7	(a) 50	(b) 50.1	(a) 7.4	(b) 7.6	(a) 470	(b) 475	(a) 15.6	(b) 15.8
	(c) 110.0		(c) 73.7		(c) 7.3		(c) 490		(c) 15.8
	(d) 92.8		(d) 55.2		(d) 7.3		(d) 490		(d) 16.2

RELATIONS OF BODY FLUID TO THE SEIZURE

During this study a total of twenty-eight convulsions occurred, which were distributed among nine patients. An attempt was made to analyze

the status of the body fluids before and after the seizure. The studies on blood chemistry were obtained at varying periods, and hence the intervals before and after the individual convulsions differed widely. In general it may be stated that in the present study the results were too inconstant to permit any conclusions as to the relation of body water to the convulsion (table 4).

COMMENT

McQuarrie, Gamble, Jacobsen, Clegg and Thorpe and others have reported that the incidence of convulsions is increased with high fluid intake with and without pitressin, whereby it has been assumed that a state of hydration is produced. An increase in body weight was their chief indication of a state of hydration. In our studies only one patient in a group of thirteen had a convulsion during the so-called period of hydration and not in the period of control or of "dehydration." In four other cases seizures occurred not only during "hydration" but in one or both of the other periods. Changes in body weight as a result of forced fluid intake and pitressin were inconstant and in our opinion were not a true index of the production of a state of hydration. Furthermore, studies on blood chemistry and body fluid failed to give satisfactory findings to verify the assumption that hydration was produced by this measure. Analysis of the reports of other investigators who have carried on similar studies reveals no critical evidence that a state of hydration was obtained. As pointed out earlier in this presentation, the common practice of estimating water balance by comparing the output of fluid (as the volume of urine) with the intake is extremely inaccurate. Many writers have accepted a gain in weight following administration of fluids and pitressin as evidence of hydration. If this is true, in half our cases we were unable to produce a state of hydration; it seems to us, however, that increase in weight does not constitute proof of a state of hydration. Furthermore, it is difficult to control the many variable factors contributing to the weight obtained at any given time.

In dehydration loss of weight is commonly reported. With such reports our findings are in accord. Again, however, more critical evidence of a negative water balance should be provided by determinations of blood volume and blood chemistry, analysis of body fluids and other methods not available at this time. Few such careful studies are to be found in the literature. In the present study evidence of concentration of the blood and a fall in the blood volume and the total body fluid is fairly constant, but contradictory findings occurred in several instances. Our realization of the inadequacy of present methods of examination has led us to be cautious in the interpretation of such data.

CONCLUSIONS

1. The water metabolism of the epileptic patient under ordinary circumstances, as revealed by the ratios of fluid intake and fluid output, hematocrit readings, and the determinations of blood volume, plasma volume, blood halides (chlorides) and body fluid, shows no significant departure from the normal.

2. A high fluid intake for forty-eight hours, with or without the addition of an antidiuretic (pitressin), did not produce an increase in the incidence of convulsions in this group of adult epileptic patients. The occasional occurrence of a seizure following ingestion of a large amount of fluid may or may not be an expression of altered water metabolism.

3. It is extremely difficult to produce a state of positive water balance in the adult human subject by excessive intake of fluid supplemented by antidiuretic measures as determined by the present methods of examination.

4. There is no evidence in our study to support the contention that in the adult epileptic patient the body fluid reaches a high peak just before a convulsion, drops during the fit and rises again as a result of water retention. The epileptic convulsions are not attended by any significant alteration in the gross amount of body fluid as revealed by the present methods of examination.

5. Convulsions continue to occur in epileptic patients under a regimen of markedly restricted fluid intake for a short time, i.e., for forty-eight hours or more. Production of a state of dehydration is difficult to accomplish as estimated by the commonly employed tests. Whether with the patient under a prolonged regimen of restricted fluid intake a state of dehydration is produced and whether this dehydration tends to diminish or prevent the occurrence of convulsions remain to be proved.

Case Reports

PSYCHOSES COMPLICATING RECOVERY FROM EXTRACTION OF CATARACT

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Psychoses complicate recovery from operations for cataract fairly frequently. Various authors [1] have stated that serious mental disturbances occur in approximately 3 per cent of all cases in which an operation is performed. Although statistical evidence is not available, one gains the impression from a review of the literature that psychoses are more frequent in ophthalmologic than in general surgical practice.

Surgeons [2] have emphasized that a severe mental disturbance after an operation on the eye constitutes a grave danger to the patient. It is customary to bandage both eyes after operation; so an excited patient is apt to injure himself by falling out of bed or by colliding with objects in the room. The eye which recently has been operated on is in an extremely delicate condition. It may be irreparably damaged if the intra-ocular pressure is raised by sudden movement or if the dressings are torn off by the disturbed patient.

The psychiatric complications of ophthalmologic surgical procedures seem, therefore, to be of considerable clinical importance. In view of this fact it is somewhat surprising that the literature dealing with the subject is so incomplete. The papers by Parker [1a] in 1913, Brownell [1b] in 1917 and Greenwood [1c] in 1928 are, so far as we are aware, the only publications in English of studies of representative groups of cases. Psychiatrists seem either not to have concerned themselves with the subject or not to have had the opportunity to study the psychiatric problems which arise in ophthalmologic wards. Ophthalmologists, on the other hand, apparently have not attempted to apply the criteria of modern clinical psychiatry to the available material. This has resulted in the loose application of such indefinite terms as delirium, acute mania, dementia and insanity, with consequent confusion in the evaluation of the etiology, prognosis and treatment of these psychoses.

In this report four cases of psychoses complicating recovery from operations for cataract are discussed in some detail. They illustrate various aspects of the clinical psychiatric problem.

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1. (*a*) Parker, W. R.: Postcataract Extraction Delirium: Report of Eleven Cases, J. A. M. A. **61**:1174 (Sept. 27) 1913. (*b*) Brownell, M. E.: Cataract Deliriums, J. Michigan M. Soc. **16**:282 (June) 1917. (*c*) Greenwood, A.: Mental Disturbances Following Operations for Cataract, J. A. M. A. **91**:1713 (Dec. 1) 1928.

2. (*a*) Bruns, H. D.: After-Treatment of Cataract, Ann. Ophth. **25**:718 (Oct.) 1916. (*b*) Greenwood.[1c]

REPORT OF CASES

CASE 1.—*History.*—A. N., a married Swedish man aged 67, was admitted to the ophthalmologic service of the New Haven Hospital on March 25, 1935, complaining of failing vision.

One brother was said to have become insane while ill with a tumor of the neck; no details were available. The brief family history was otherwise negative for major psychiatric illnesses.

The patient was born in Sweden. No data covering his early life were available. He described his adult personality as cheerful and not subject to nervous or emotional upsets. He said that others had always considered him intelligent. For thirty-five years he had earned a steady living as a mill hand. After this he had worked for ten years as a night watchman until failing vision forced him to give up work. At no time had he used alcohol to excess.

The patient's health had been good until 1924, when he was 55 years of age. At that time appendectomy had been performed, with uneventful recovery. In 1932, when he was 64, an episode of acute urinary retention occurred, which was treated by catheterization and an abdominal operation, the details of which were not available. There had been no subsequent symptoms of urinary disturbance. Later in 1932 a carcinoma of the right side of the jaw had been diagnosed and treated successfully (?) by irradiation and implantations of radium. A complete review of the systems otherwise gave negative results.

The patient had worn glasses for eleven years because of cataracts. For nine years vision in the right eye had been entirely lost. In February 1935, six weeks before admission to the hospital, vision in the left eye began to fail noticeably. Neither eye had been injured or infected. A diagnosis of bilateral senile cataracts was made. Operation was advised and was acceptable to the patient.

Physical Examination.—On admission the temperature, pulse and respiratory rate were normal. The blood pressure was 154 systolic and 70 diastolic. Senile cataract was present on both sides, mature in the right eye and immature in the left eye. The nutritional condition was good. There was complete adentia. A small red mass was noted in the mouth at the angle between the right mandible and the maxilla, which was not inflamed or tender. There was no regional adenopathy.

Laboratory Examinations.—The hemoglobin content and the white and red blood cell counts were within normal limits. Urinalysis gave negative results except for a faint trace of albumin. The Kahn reaction of the blood was negative.

Mental Status.—The patient was friendly, cheerful and cooperative on admission to the hospital. No confusion or emotional disturbance was observed.

Course in the Hospital.—On March 25, the evening of admission, phenobarbital 0.1 Gm. (1½ grains) was given and the patient slept soundly. The morning of March 26 was uneventful. Phenobarbital 0.1 Gm. (1½ grains) and codeine sulfate 0.064 Gm. (1 grain) were given as a preoperative sedative. At 2 p. m. the cataract in the right eye was extracted without difficulty with the area under local anesthesia with cocaine and procaine hydrochloride. The patient cooperated well during the operative procedure, and was returned to the ward in good condition with both eyes bandaged. A special nurse was assigned to the case, and he was in a single room. The nights of March 26 and March 27 were uneventful. He slept well without sedatives, although he complained of slight discomfort in the eye which had been operated on. On March 27 he was comfortable all day. Food and fluids were taken well, and urine was voided satisfactorily. Phenobarbital

0.1 Gm. (1½ grains) was given at 10 p. m., and he had a comfortable night. The morning of March 28 was uneventful; he ate a good lunch at 12:30 p. m. Both eyes were still bandaged, and the special nurse was still on duty. At 1 p. m. she left him alone for the first time.

When the surgeon entered the room at 1:45 p. m. to do the first dressing, he found the patient in a highly disturbed condition. He was said not to have known where he was. He trembled and appeared frightened, saying that he was blind and would never be able to work again and that he was going to die. He wanted to go home and tried to get out of bed. The bandage was removed from the untreated eye, and special nursing care was resumed.

The patient was seen for the first time by the psychiatric consultant at 2:30 p. m. He was moving restlessly in bed and seemed apprehensive. The temperature and the respiratory rate were normal, but the heart rate was 108. Orientation was correct for time, place and person. He complained that a powerful radium machine had been placed in the room and that the doctor had fooled him by not telling him they planned to use the machine on him. There was evidence of auditory illusions. He said: "Make those people out there stop talking." Memory for recent events was good except for the immediate situation, and there was no evidence of clouding of consciousness. He said that he had not been apprehensive before the operation. He had begun talking about the radium machine at the time when the clattering dressing cart had been wheeled into the room. This was explained to him, but he refused to believe it. At 3 a. m. he was given phenobarbital 0.1 Gm. (1½ grains). He was comfortable the rest of the day, ate a good supper and went to sleep quietly. About 9 p. m., however, he said that he thought the nurses were trying to poison him and that he wanted to go home. He was given sodium amytal 0.1 Gm. (1½ grains) and codeine sulfate 0.064 Gm. (1 grain). He remained quiet until 3:30 a. m. on March 29, when he again became restless and tried to get out of bed. The dose of sodium amytal and codeine sulfate was repeated, and he slept quietly the rest of the night. He ate a good breakfast and was comfortable during the morning.

The patient was seen for the second time by the psychiatrist at 2 p. m. on March 29. At that time the mental disturbance showed distinct improvement. No disorientation or significant defect of memory was present. He gave an interesting retrospective account of his disturbance during the preceding two days. He said that while he lay drowsing on the night of March 27 and March 28 with both eyes bandaged, he had seen quite clearly a garden covered with snow. He himself was moving about the garden but leaving no tracks in the snow. This experience was so vivid that he had groped around in the darkness feeling the bed to be sure he really was in the hospital. A few minutes later he had seen people grouped around the foot of the bed making faces at him and again had groped about in the darkness wondering where he was.

On the morning of March 28, while his eyes were still bandaged, the patient had felt a peculiar sensation all over his body as if a radium machine were being used on him. He also had heard people snoring in the room. He had repeatedly asked the nurse what was going on. He was told that nothing was going on and to put his head back and rest. He did not recall having become disturbed in the early afternoon of March 28. His attitude toward the reality of his experiences fluctuated. At times he referred to the radium machine as real. A few minutes later he would laugh and say that it must have been his imagination. His general attitude was friendly and in no way suspicious.

The subsequent course in the hospital was entirely uneventful, and the patient was discharged in good condition on April 1, 1935.

Comment.—In this case the patient, a man aged 67, apparently had made a normal adjustment to his environment previously. He had experienced two major surgical procedures uneventfully, and even the diagnosis of cancer had not disturbed him objectively. During his brief psychosis, however, there was evidence in his content of thought of the deep impression that the treatment of the malignant growth had made on him. Although a moderate degree of arteriosclerosis was present (which presumably involved the cerebral vessels to some degree), there was no evidence that significant deterioration of personality had occurred. Like the next patient presented, he had accepted the loss of vision in a normal way and had not been alarmed at the prospect of an operation. On the second postoperative day, however, in a setting of darkness, a typical state of panic developed, characterized by experiential confusion, with paranoid misinterpretation of the environment. No factors were present which would account for organic delirium, and the clinical picture seemed to be a purely psychogenic (experiential) disturbance. The content of thought was, of course, colored by his previous experiences with radium. The psychosis subsided within twenty-four hours after the removal of the bandage from the untreated eye. The residual mental status was normal.

CASE 2.—*History.*—C. R., a single Irish woman aged 56, was admitted to the ophthalmologic service of the New Haven Hospital on April 8, 1934, complaining of failing vision.

The brief family history included no mention of major psychiatric illnesses.

Details concerning her personality development and adult adjustment were not available. She had earned a modest but steady living all her life as a domestic servant and had never been in emotional difficulty.

The past medical history, including a detailed review of systems, was without significance. The patient had passed the menopause at 43 without difficulty. Physical examination in the medical outpatient clinic in 1930 had revealed myomas of the uterus which were not causing symptoms and for which no treatment was advised. The blood pressure at that time was 150 systolic and 112 diastolic. No significant arteriosclerosis was noted.

A high degree of myopia had been present for many years, for which the patient had worn corrective lenses. In 1930 immature senile cataract of each eye was discovered. An iridectomy was done on the right eye preparatory to extraction of the cataract. She stood the operative procedure well, and no mental disturbance developed while she was in the hospital. She had been practically blind in the left eye since 1930, and vision had continued to fail in the right eye until she could see only the vague outlines of persons and the lettering on large sign boards. In April 1935 extraction of the cataract from the right eye was advised. This was acceptable to her.

Physical Examination.—On her admission to the hospital the temperature and the respiratory rate were normal. The heart rate was 100, but it quickly returned to normal. The patient's general appearance was somewhat obese and florid. The blood pressure was 148 systolic and 90 diastolic. Both eyes were highly myopic. Senile cataract was present on both sides, mature on the right and immature on the left. The left retina was partially detached. No sclerosis of the radial arteries was noted. The uterus was myomatous.

Laboratory Examinations.—The hemoglobin content and the red and white blood cell counts were within normal limits. Urinalysis revealed no abnormal findings. The Kahn reaction of the blood was negative.

Mental Status.—The mental condition on admission attracted no special attention. The patient was entirely cooperative toward nursing procedures during her first day in the hospital.

Course in the Hospital.—In the evening of April 8 the patient was given phenobarbital 0.1 Gm. (1½ grains), two tablets of a mixture of allylisopropyl barbituric acid and aminopyrine and acetylsalicylic acid 0.6 Gm. (10 grains) as a sedative. She had a comfortable night and slept well. The next morning, April 9, phenobarbital 0.1 Gm. (1½ grains) and codeine sulfate 0.064 Gm. (1 grain) were administered as a preliminary sedative, and at 3 p. m. the cataract was extracted from the right eye without difficulty with the area under local anesthesia with cocaine and procaine hydrochloride. She was cooperative throughout the procedure and was returned to the ward in good condition with both eyes bandaged. A special nurse was on duty. During the same afternoon and evening she complained of occasional pain in the eye which had been operated on, for which she was given codeine and acetylsalicylic acid on several occasions. There were no postoperative elevation of temperature and no tachycardia. Food and fluids were taken well, and urine was voided satisfactorily. She was comfortable on April 9 and April 10, but at 3 a. m. on April 11 the nurse noted that she seemed somewhat alarmed about her condition. After reassurance she fell asleep and spent a comfortable day. In the early morning of April 12, however, she was apprehensive and worried and kept calling for her brother. She complained of dizziness, which was relieved by lowering the head of the bed. During the same afternoon she was somewhat noncooperative toward nursing procedures and insisted that she was not sick. She refused medication, saying that the nurse was trying to put her back to sleep. According to the nurse, she was disoriented, but no definite evidence was recorded to support this opinion. Toward evening she said that she thought the nurse was trying to hide things so that she would not be able to find them.

The psychiatric consultant saw the patient for the first time at 7 p. m. on April 12. She was lying quietly in bed, comfortable and cooperative. The temperature, respiratory rate and heart rate were normal. Orientation was correct for time, place and person. There was no impairment of recent or remote memory. Her grasp of general information was about what would be expected of a person of her station in life. She recalled the details of her admission to the hospital and discussed her present complaints without difficulty. She said she had been turned around in bed that morning with her head placed at the foot of the bed. This was true. Then she had not known where she was, had become frightened and had tried to find out what had happened to her. She had felt uncomfortably warm and had wanted to sit up to talk to her physician. No special emotional display was noted during the interview, and it was easy to reassure her. She said she realized that it was necessary to keep her eyes bandaged for a while and that this was part of the treatment. No evidence of hallucinations or illusions was obtained.

The bandage was removed from the untreated eye later that day. The subsequent psychiatric course was entirely uneventful. On April 17 there was a temporary fall of blood pressure from 140 to 98 systolic and from 98 to 68 diastolic, with some accompanying dyspnea. This condition responded well to stimulation, however, and the patient was discharged from the hospital in good condition on April 23, 1934.

Follow-Up.—On Aug. 19, 1935, it was noted in the ophthalmologic outpatient clinic that her vision had not improved sufficiently to warrant prescribing glasses. Her mental condition did not arouse comment.

Comment.—The clinical situation seen here resembles closely that observed in the first case. The patient, a woman aged 56, had previously made a normal, modest adjustment to life. She had experienced the climacteric period and had been told that she had high blood pressure without showing any abnormal emotional display. She had not worried, nor had she become depressed over the loss of vision, and she had accepted tranquilly the prospect of an operation on her eye. There was no reason to believe that she would show any abnormal personality manifestations during her period of care in the hospital. Nevertheless, on the second postoperative day there developed a definite state of low grade panic. No factors were present which would account for organic delirium (symptomatic psychosis), nor did the clinical picture suggest an organic cerebral disturbance. It would seem that this simple woman in an unfamiliar setting of darkness became apprehensive, somewhat suspicious and experientially confused. The disturbance was apparently purely psychogenic (experiential). The symptoms subsided rapidly after reassurance and the removal of the bandage from the untreated eye. The residual mental status was normal.

CASE 3.—*History.*—N. G., a widowed woman of the older New England stock, aged 83, was admitted to the ophthalmologic service of the New Haven Hospital on Dec. 10, 1934, complaining of failing vision.

The brief family history included no mention of major psychiatric illnesses.

The patient had always been considered energetic and fairly well adjusted to her environment but had been nervous and definitely excitable in certain situations. Her husband had died several years previously without any unusual reaction on her part. Since that time she had lived alone in a furnished room. Her past medical history was essentially without significance.

For about fifty years the patient had worn glasses bought in a 10 cent store. During the past five years the development of cataracts had led to progressive failure of vision in both eyes. Several years before her admission to the hospital operation had been advised but had been refused by the patient. Increasing visual difficulty finally led her to consent to an operation, but she was much afraid of it. Before leaving for the hospital she wrote a note requesting friends to investigate the situation if she failed to return home after the operation. This fact was not known to the ophthalmologic service at that time.

Physical Examination.—On admission the temperature and respiratory rate were normal. The heart rate was 100, but the acceleration was not constant. The blood pressure was 164 systolic and 84 diastolic. The general appearance was senile, but she seemed younger than her stated age of 83. Bilateral senile cataracts were present, mature in the left eye and immature in the right eye. The skin was flabby. The radial arteries were definitely sclerotic. There was weakness of the lower right side of the face.

Laboratory Examinations.—The hemoglobin content and the red and white blood cell counts were within normal limits. Two urinalyses showed definitely positive reactions for albumin. The Kahn reaction of the blood was negative. The blood sugar content was 84 mg. per hundred cubic centimeters, nonprotein nitrogen 58 mg. per hundred cubic centimeters.

Mental Status.—On admission the patient was excited and apprehensive about the coming operation. Acceleration of the heart rate to 100 per minute was noticed on several occasions during her first day in the hospital.

Course in the Hospital.—The evening of admission, December 10, was uneventful. Sodium bromide 2.6 Gm. (40 grains) was given as a sedative, and the patient spent a comfortable night. The morning of December 11 was also uneventful, and at 2 p. m. the cataract was removed from the left eye with the area under local anesthesia with cocaine and procaine hydrochloride. She behaved well during the operative procedure and was returned to the ward in good condition with both eyes bandaged. She occupied a single room. A special nurse was not assigned to the case. She did not complain of pain and ate a good dinner. At midnight she complained of nausea and was observed to be sweating. Morphine sulfate 0.01 Gm. (⅙ grain) and atropine sulfate 0.0003 Gm. (1/150 grain) were given. She slept quietly the rest of the night, but on the morning of December 12 she was slightly nauseated after eating a light breakfast. Urine was voided satisfactorily. She vomited a small amount of food after the noon meal but rested quietly for the rest of the day and took her evening meal fairly well. In the afternoon she seemed much pleased when the attending surgeon informed her that she was doing well. That night, however, when the floor nurse entered the room at 7:30 p. m., she found the patient sitting upright in bed, excited and apprehensive of impending bodily harm. She refused a sedative and ordered the nurse from the room. She was restless and talked rapidly, complaining of noises in the corridor. She misinterpreted the hospital loud speaker, saying that her name was being called to tell her that she was to be taken to the cellar and put into a box. Reassurance by the house surgeon quieted her temporarily, but at midnight she was disturbed again. She complained of smelling ether and said some one was coming in through the door after her. She attempted to get out of bed, but reassurance again quieted her. During the early part of the night the disturbance continued. At times she spoke of people being in the room trying to do something to her. She continually picked at the bedclothes and clutched at herself. She slept finally until 7 a. m. on December 13, but again was disturbed on awakening. At 10 a. m. the bandage was removed from the untreated eye, and she was seen by the psychiatric consultant.

Orientation was correct for time, place and person, and there was no evidence of clouding of consciousness or defect of memory. The temperature and respiratory rate were normal. The heart rate was 130. She was highly suspicious and did not want to talk to the psychiatrist. She drew away from him saying that he might hurt her. She was highly apprehensive, thinking she was to be taken to the basement to be "gotten rid of." People in the corridor were talking about her. She was sarcastic, irritable and evasive about her paranoid ideas, but by appealing to her vanity it was possible to talk to her fairly satisfactorily. She told of a dream in which a nurse had entered the room with a flashlight, firing a pistol at her. Since the operation her temperature had remained normal; she had taken fluids fairly well, and had voided urine satisfactorily.

She was not given any sedative. During the night of December 13 and also during the night of December 14, she was again excited and apprehensive at intervals. Several times she attempted to get out of bed and called loudly for help. She responded fairly well to reassurance, however. She ate breakfast satisfactorily on December 14 and from that time on the mental disturbance gradually faded, although a definitely suspicious attitude remained. She was sarcastic, irritable and generally suspicious toward nursing procedures. In the afternoon of December 14 she was presented at a teaching psychiatric clinic. At that time her memory

for both remote and recent events, including the period of mental disturbance, was good. She refused to elaborate on her recent experiences but obviously enjoyed holding the center of the stage.

On December 18 she was discharged in good condition.

Comment.—In contrast with the two patients previously discussed, this woman had been emotionally unstable all her life. She had been definitely apprehensive and suspicious concerning the proposed operation. Although no actual deterioration had occurred, her personality had developed into a rigid, senile mold. It might reasonably have been anticipated that some degree of disturbance of personality might occur during the postoperative period. A severe state of panic developed acutely twenty-nine hours after operation in a setting of darkness and was characterized by experiential confusion, with paranoid misinterpretation of the environment. No factors were present to account for organic delirium, nor did the clinical picture resemble such a condition. The entire acute disturbance was apparently psychogenic (experiential), although seen against a background of senile rigidity in an emotionally unstable personality. The acute psychosis subsided within forty-eight hours after removal of the bandage from the untreated eye. The residual picture, however, resembled that observed before operation. She was egocentric and suspicious and emotionally somewhat childish.

CASE 4.—*History.*—A. H., a married Swedish man aged 74, was admitted to the ophthalmologic service of the New Haven Hospital on Sept. 26, 1935, complaining of failing vision.

No detailed family history was available.

Neither the patient nor his wife was able to give any history of his early development. As an adult he was said to have been friendly and cheerful and to have adapted himself comfortably to his environment. The brief personality history suggested gradual deterioration for several years before admission. Episodes had occurred which seemed to indicate intermittent confusion, especially at night. For example, on one occasion he had wandered into a coal bin at night with a lighted candle and had not been able to offer any satisfactory explanation for his conduct. For many years he had worked steadily as a cabinet maker until advancing age and loss of vision obliged him to retire.

It was impossible to obtain the past medical history in detail because of the patient's extreme circumstantiality. His health was said to have been good up to the past few years. Eighteen months before admission to the hospital he had fractured several ribs and had made an uneventful recovery. Four months before admission he had sustained minor burns of his right thigh.

He had worn glasses for close work since 1925. In 1933 definite but gradual loss of vision in both eyes had begun. A few months before admission he no longer was able to get about the house and could not read even large newspaper type. There had been no headache, pain in the eyes or diplopia. A diagnosis of senile cataract on both sides was made in September 1935, and operation was advised. This was acceptable to the patient.

Physical Examination.—The temperature, heart rate and respiratory rate were normal. The blood pressure was 136 systolic and 88 diastolic. The general appearance was senile. Bilateral senile cataracts were present. There was complete adentia. The radial arteries were definitely sclerotic.

Laboratory Examinations.—The hemoglobin content and the white and red blood cell counts were normal. Urinalysis gave negative results. The Kahn reaction of the blood was negative.

Mental Status.—On admission the patient was friendly and cooperative. He wanted an operation done to improve his vision and did not seem afraid of it. Orientation was correct for time, place and person. He was garrulous and circumstantial. The stream of thought was definitely wandering, so that he was able to give only the barest outline of his history. No formal test for memory was given.

Course in the Hospital.—The night before the operation the patient was given sodium amytal 0.2 Gm. (3 grains) and slept well. He was comfortable the following morning and received no additional sedative before going to the operating room. The cataract was extracted from the right eye without difficulty, with the area under local anesthesia with cocaine and procaine hydrochloride, at 4:30 p. m. on September 27. He was cooperative throughout the procedure and was returned to his room in good condition with both eyes bandaged. A special nurse was assigned to him, and one other patient was in the room. At 8:00 p. m. he was very restless. He tried to get out of bed and seemed confused. At 11:00 p. m. he was given sodium amytal 0.2 Gm. (3 grains) and codeine sulfate 0.032 Gm. (½ grain). At 12:10 a. m. on September 28 he vomited and his pulse was somewhat irregular. The same dose of sodium amytal and codeine sulfate was repeated, but he continued to be very talkative and restless all night. During the morning and afternoon of September 28 the same situation continued. There had been no postoperative elevation of temperature. He took fluids well and voided urine satisfactorily. At intervals he seemed restless, unduly talkative and confused. Additional doses of codeine sulfate 0.032 Gm. (½ grain) were given at 9:45 a. m. and 4:25 p. m. The bandage was removed from the untreated eye at 5:45 p. m.

The patient was seen for the first time by the psychiatric consultant at 7:15 a. m. on September 28. At that time he was lying quietly in bed. He was completely disoriented for time, place and person. He said that it was August 1932, that he was in Thomaston (his home town), that he was in his own house and that he wanted to go down to the cellar. He could not tell why he was in the hospital except that he was a "damned fool." He was unable to identify the bandage on his eye as such and could not recall having been operated on. He was talkative; the stream of speech was rapid and lacking in coherence and direction. The temperature and the respiratory rate were normal. The heart rate was 76. The emotional status was normal. He was pleasant and friendly and definitely not fearful or apprehensive, although somewhat restless. He was so confused that it was impossible to give any formal tests for recent or remote memory, and he was unable to give a coherent account of his present situation. No delusional trend was manifested, and no evidence of hallucinations or illusions was obtained.

No additional sedatives were given. Confusion continued through the night of September 29 and 30. On several occasions the patient tried to get out of bed. Some abdominal distention was noted, but he continued to void urine satisfactorily. The quality of the pulse had improved.

He was seen again by the psychiatrist at 9:30 a. m. on September 30. At that time his mental condition showed great improvement. Attention was good. Distractibility was normal. Orientation was correct for time, place and person. Three minute retention was slightly impaired. His account of events in his rather remote past was fairly adequate but lacking in detail and highly circumstantial.

His description of the recent period of disturbance was hazy, and he showed no insight concerning it, saying that he had tried to get out of bed merely to get his clothes. There was no emotional disturbance. He was friendly and cooperative and promised not to disturb the bandage on his eye.

At 2:30 p. m. on September 30 the patient became confused again and excitedly demanded his clothes, saying that people might harm him if he did not get them. Episodic confusion continued through the night of September 30 and October 1. At 2:00 a. m. on October 1 he was given 10 cc. of paraldehyde and slept fairly well until about 7:00 a. m., when he seemed restless and confused again.

The patient was seen again by the psychiatrist at 11:00 a. m. on October 1. He recognized his visitor as a physician but could not recall his name. He was disoriented for time and place, saying that it was the year 1693 and that he was in Sweden. He wanted to see Dr. B. (the attending ophthalmologist) in New Haven, although he still thought he was in Sweden. No paranoid trend was demonstrated. The heart rate was normal. His emotional state showed no disturbance. The stream of speech was rapid, mumbled and incoherent. He showed no insight, saying that he wanted his clothes brought because he always was at work by half past nine in the morning.

No further change occurred in the patient's condition until his discharge from the hospital. No elevation of temperature occurred. He took food and fluids well and voided urine regularly. Sedatives were not required, but it was necessary for a special nurse to remain with him constantly. Episodic confusion was noted repeatedly. This did not seem to bear any relation to external settings and occurred about as frequently during the day as during the night. No definite paranoid trend developed, and no evidence of hallucinations or illusions was obtained. If he was held back when he attempted to get out of bed he became momentarily alarmed. He never attempted to injure his eye, which healed nicely. On October 12 he was discharged from the hospital in a satisfactory condition from the ophthalmologic point of view. Psychiatrically his memory was defective and episodic confusion was still present.

Second Admission.—At home he adjusted comfortably and was much pleased by the improvement in vision in his right eye. He was desirous of having his left eye treated also, and therefore on Jan. 15, 1936, he was readmitted to the ophthalmologic service.

Physical Examination: The findings were described as being the same as those noted at his first admission. The temperature, heart rate and respiratory rate were normal. The blood pressure was 140 systolic and 90 diastolic. A mature senile cataract was present in the left eye.

Laboratory Examinations: The hemoglobin and white and red blood cell counts were normal. Urinalysis gave negative results.

Mental Status: The patient was seen by the psychiatric consultant on the morning of January 16 before being operated on. The mental picture was the same as at the time of his discharge from the hospital in October. He was quiet, friendly and cooperative. He expressed pleasure at the favorable result of the first operation and said that he was looking forward to having his other eye attended to. He smilingly expressed the hope that he would not "go off his head" again. When questioned he said that his relatives had told him that he had been out of his head after his first operation. He could not recall the details of his mental disturbance, however. A grave sensorial intellectual defect was again easily demonstrated. He knew that it was January, but he was unable to give

the date, the day of the week or the year, even approximately. He could not recall any details concerning his first period of hospitalization but offered as an excuse the fact that he had not been able to see as well then as he could now.

It was predicted that he would cause considerable difficulty during the postoperative period. All observers agreed, however, that the operation was definitely indicated and that with adequate nursing care he probably could be managed satisfactorily.

Course in the Hospital: On the night of January 15 the patient received 1.2 Gm. (20 grains) of sodium bromide. On January 16 at 4:00 p. m. the cataract was extracted from the left eye with the area under local anesthesia with cocaine and procaine hydrochloride. He was somewhat noncooperative during the surgical procedure but was returned to a single room in satisfactory condition. A nurse was in constant attendance during the postoperative period. The bandage was removed from the untreated eye after twenty-four hours. Urine was voided satisfactorily. The temperature, pulse and respiratory rate remained normal during his entire time at the hospital. No further sedatives were employed. In spite of these precautions, however, the same type of psychotic behavior occurred as had been observed after the first operation. Restlessness and intermittent confusion were repeatedly observed. He never showed any insight into the situation. When questioned, he was unable to remember any abnormal behavior. His emotional state was tranquil except when he was prevented from getting out of bed in his episodic periods of restless confusion, at which times moderate excitement was observed. At no time did he try to injure his eye. Although the mental condition showed no improvement, surgical recovery was uneventful and he was discharged from the hospital on January 25.

Comment.—The condition in this case falls into a clinical group entirely different from that of the first three. This man had shown before operation definite evidence of a deteriorative organic psychosis due to cerebral arteriosclerosis. It might have been predicted almost with certainty that he would present a grave problem in postoperative management. The symptoms after operation were those present before, namely, clouding of consciousness, organic disorientation and defect of memory. The general postoperative situation doubtless exaggerated the symptoms to some degree in a psychogenic way, but the total picture was one of organic delirium, not psychogenic (experiential) panic. Removal of the bandage from the untreated eye was without effect. When he was discharged from the hospital, symptoms of organic deterioration were still readily demonstrable. Three months later, at the time of the second operation, the psychotic symptoms were equally severe, although every effort was made to reassure him before operation and to make him comfortable during the postoperative period.

GENERAL COMMENT

In the first three cases a diagnosis of psychogenic (experiential) panic was made. By panic is meant an acute reactive affective disturbance, objectively manifested as restlessness and subjectively experienced as fear. The importance of psychogenic (experiential) factors in many of the psychoses complicating extraction of cataract has been emphasized in previous reports. In this small group of cases psychogenic (experiential) factors seemed definitely more conspicuous than

in most psychoses arising as complications of somatic disease. Two psychologically valid reasons for this are at once apparent: first, the age of the patients operated on, and second, the emotionally disturbing effect of the postoperative setting of darkness.

It is common knowledge that the aging personality tends to become increasingly more rigid. Elderly persons adjust poorly to changes in the environment, and they readily become emotionally upset when confronted by new and difficult situations, especially if these are poorly comprehended and are associated with feelings of insecurity. Bruns [2a] has emphasized especially clearly the importance of the age of the patient in the psychoses complicating extraction of cataract. It should be stated, however, that at this point the aging process is being considered only in its experiential aspect, not in the sense of senile-arteriosclerotic encephalopathy with sensorial-intellectual defect.

Both ophthalmologists and psychiatrists have long been aware that the bandaging of both eyes, leaving the patient in total darkness more or less isolated from his environment, is peculiarly apt to produce a profound loss of security and orientation, with consequent experiential confusion, fear and excitement. In many cases this factor alone seems sufficient to precipitate a psychotic episode, as is demonstrated by the rapid recoveries frequently observed after the untreated eye is uncovered. Naturally the resolution of symptoms does not occur with equal rapidity in all cases. Obviously psychopathic, emotionally unstable persons, such as the third patient presented in this report, respond less readily to favorable alteration of the environment. We believe, however, that the majority of the cases in which definite improvement does not occur within two days after the bandage has been removed and quieting reassurance has been given will be found on critical evaluation to belong to entirely different clinical categories. Not all the psychoses observed as complications following extraction of cataract are psychogenic panics.

This fact appears to have escaped the attention of some authors and accounts for many of the conflicting statements in the literature concerning the etiology, prognosis and treatment of these psychoses. One would not reasonably expect that all the psychoses observed as complications of extraction of cataract would be of the same etiology. Senile and arteriosclerotic psychoses are observed occasionally in any unselected group of elderly patients. The characteristic picture is one of chronic, organic, sensorial-intellectual defect, with fluctuating disorientation and impairment of memory in the absence of striking emotional disorder. Such a picture is readily distinguishable from a typical psychogenic state of panic and is well illustrated by the fourth case reported. In this organic type of psychosis the operation plays no etiologic rôle. It creates, however, a difficult problem of operative and postoperative nursing care, and it is therefore important to recognize its existence before operation is undertaken. The type of behavior which may be expected of such patients is well illustrated by our fourth patient. Frequently, of course, cases are observed in which both organic and experiential factors play important etiologic rôles in the psychosis. The patient with senile-arteriosclerotic encephalopathy is much more liable to be

disturbed by environmental stress than is the normal person. Because of the organically conditioned difficulties in orientation, comprehension and memory, attitudes of suspicion and apprehension are likely to develop. A working understanding of such a patient's psychosis cannot, however, be obtained from a consideration of either the organic or the experential aspect alone. Both factors must be evaluated etiologically and both must be taken into consideration in treatment.

Lastly, the ophthalmologic surgeon may occasionally—fortunately not frequently—encounter manic-depressive and schizophrenic psychoses. In rare instances the operation may act as a precipitating factor for such psychoses. In most cases, however, the psychosis will be found either to have existed before the operation was undertaken or to have developed after a considerable latent period, not in any etiologic relationship to the surgical procedure. The recognition of a manic-depressive or a schizophrenic psychosis before operation is, of course, important, as such conditions are usually contraindications to any elective surgical procedure. The problems of prevention, prognosis and treatment are more easily approached if the chief etiologic factors already outlined are kept in mind.

Many of the psychogenic disturbances are preventable, as Bruns [2a] has shown especially clearly. This author reported a series of two hundred and seventy-two consecutive cases of extraction of cataract in which the patient was treated on a strictly ambulatory basis, without the occurrence of a single psychosis. He emphasized that allowing the patient to return to the familiar, friendly surroundings of his own home immediately after operation eliminates many of the psychologically undesirable factors from the postoperative situation and so tends to prevent the occurrence of psychosis. Bailey's [3] experience was similar. He reported entirely satisfactory surgical and psychiatric results from the routine extraction of cataract in the patient's own home. In his opinion this method greatly simplifies the problem of postoperative care. Psychiatrists realize that practical surgical difficulties no doubt prevent general adoption of the methods of management employed by Bruns and Bailey. The experiences of these surgeons, however, confirm the opinion that psychologic factors are of the greatest importance in the prophylaxis of these psychoses. Greenwood [1c] discussed the application of prophylaxis in the hospital environment. He stressed the importance of evaluating the patient's mental condition before operation and of allaying his fears in advance by carefully conducted reassuring discussions. Special care should be taken to explain the meaning of all procedures and examinations lest the patient be alarmed by them. During the postoperative period small amounts of morphine and scopolamine should be given to prevent pain. In Greenwood's opinion, constant nursing care is (psychiatrically) indispensable during the time when both eyes are bandaged. The psychiatric point of view is in agreement with that of Greenwood. The occurrence of acute psychogenic panic probably cannot be prevented in all cases, however, even though the best possible psychiatric care is given during the preoperative and the postoperative period.

3. Bailey, F. W.: Cataract Operations Performed upon Patients in Their Own Beds, J. Iowa M. Soc. **18**:8 (Jan.) 1928.

Some personalities are emotionally so unstable, either constitutionally or as a result of increasing senile rigidity, that any unpleasant or threatening situation is likely to provoke an emotional storm. The recognition of such a personality trend before operation is important. For this a brief psychiatric history is indispensable in every instance of ophthalmologic operation, taken with special reference to the patient's excitability and behavior during previous stressful situations.

The organic psychoses due to senile-arteriosclerotic encephalopathy are not preventable in the light of the present knowledge of the underlying cerebral pathologic processes. The secondary psychogenic symptoms which are sometimes observed in such cases are partially preventable by the methods which have already been discussed in reference to psychogenic panic.

Like all reactive emotional disturbances, the psychogenic panic states tend to run a self-limited course and to have a good prognosis. Spontaneous recovery will occur in most cases. The speed of recovery may be accelerated by proper psychiatric management. The senile-arteriosclerotic psychoses, on the other hand, are chronic and have a uniformly bad prognosis, terminating in most cases in profound organic deterioration. Remissions may occur, however, if adequate medical and nursing care is given, directed especially toward relieving the cardiovascular system of strain.

The treatment of the psychogenic panics should be directed toward calming the state of fear and suspicion which characterizes them. A quiet room, reassurance by the attending physician and the constant presence of an understanding, tactful nurse [4] are invaluable aids. Early removal of the bandage from the untreated eye is always desirable and in many cases absolutely necessary, as Greenwood [1c] has emphasized. Psychotherapeutic measures are of much greater importance than drugs in the management of these cases. In some instances no sedatives need be given. The danger of producing toxic delirium by the administration of sedative drugs to the elderly patient should be kept in mind. Paraldehyde in moderate doses is the sedative of choice when the use of drugs seems indicated. If a state of marked excitement is present, it may be necessary to employ small doses of morphine and scopolamine hypodermically.

No method of treatment is available to produce rapid resolution of the organically determined symptoms of the senile-arteriosclerotic psychoses. Sedative drugs not only are ineffective in the usual doses but are dangerous, since they tend to increase the clouding of consciousness which is already present. When an elective surgical procedure is undertaken in the presence of an organic psychosis, the surgeon must be prepared to encounter a difficult situation postoperatively. The constant presence of watchful attendants constitutes the greatest aid toward carrying the patient safely through the critical period until the eye has healed. Eventual improvement in the mental symptoms may occur in response to nursing care and general supportive measures.

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4. Wilson, M. W.: Nursing Care in Adult Cataract Cases, Am. J. Nursing **31**:33 (Jan.) 1931.

SUMMARY

Four cases of psychosis complicating extraction of cataract are reported.

In three cases a diagnosis of psychogenic panic was made. In the fourth case the diagnosis was organic (senile-arteriosclerotic) mental disorder.

The etiology, prevention, prognosis and treatment of psychoses complicating extraction of cataract are discussed.

The importance of the psychiatric differential diagnosis in the understanding and management of this etiologically heterogeneous group of psychoses is emphasized.

SURGICAL TREATMENT OF PINEAL TUMOR

EDGAR A. KAHN, M.D., ANN ARBOR, MICH.

Direct attack on a tumor which has arisen from the pineal body has in the great majority of cases resulted fatally. A number of instances of operative intervention for the removal of tumor projecting into the posterior part of the third ventricle have been reported, but on analyzing them it is not certain that complete removal of a tumor of true pineal origin has ever been accomplished prior to the cases reported in this paper.

The pinealoma is probably the commonest tumor of the posterior part of the third ventricle. Even though differentiation of the various tumors found here can be made only by biopsy and the operative approach is the same in all, I am considering only the tumor of true pineal origin.

A large cystic tumor was removed by Sachs [1] in 1926 from the region of the pineal gland, but its exact nature was not definitely determined. The tumor was considered by Sachs to be a form of cholesteatoma, but it is not established that it was actually of pineal origin. A large glioma was removed from the same region in 1927 by Foerster,[2] but again its origin is uncertain.

A case was reported by Van Wagenen [3] in which a pinealoma was excised by means of an approach through the lateral ventricle. A small amount of tumor, however, was left adherent to the vein of Galen. In the case of Harris and Cairns,[4] although it seemed as if all tumor had been removed, recurrence of symptoms nine months later makes this improbable.

Dandy [5] has had three cases in which the patient survived operation; two died of recurrence, and the third was alive eight months after operation. The tumor in the last case was a pinealoma, and though it was thought that it was completely excised, it is too early to say that recurrence will not take place.

REPORT OF CASES

CASE 1.—A case of pineal tumor in which operation was performed by Dr. Max Peet in 1929 was reported by Allen and Lovell.[6] At that time it was not

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From the Department of Surgery, the University of Michigan; the Clinic of Dr. Max Peet.

1. Sachs, E.: The Diagnosis and Treatment of Brain Tumors, St. Louis, C. V. Mosby Company, 1931, p. 276.

2. Foerster, O.: Das operative Vorgehen bei Tumoren der Vierhügelgegend, Wien. klin. Wchnschr. **41**:986 (July 12) 1928.

3. Van Wagenen, W. P.: A Surgical Approach for the Removal of Certain Pineal Tumors: Report of a Case, Surg., Gynec. & Obst. **53**:216 (Aug.) 1931.

4. Harris, W., and Cairns, H. W. B.: Diagnosis and Treatment of Pineal Tumors, with Report of a Case, Lancet **1**:3 (Jan. 2) 1932.

5. Dandy, W. E.: Operative Experience in Cases of Pineal Tumor, Arch. Surg. **33**:19 (July) 1936.

6. Allen, S. S., and Lovell, H. W.: Tumors of the Third Ventricle, Arch. Neurol. & Psychiat. **28**:990 (Nov.) 1932.

certain that complete removal had been obtained. The patient was a boy aged 13, who entered the University Hospital complaining chiefly of severe headaches and blurring of vision. These symptoms had appeared four weeks before admission and had become progressively worse. Two weeks later the patient began to have projectile vomiting.

Examination revealed him to be undersized, normally developed, mentally alert and well oriented. The pupils were large and equal. They were fixed to light but reacted in accommodation. The extra-ocular movements were normal, and there was no nystagmus. Examination of the fundi revealed 2 diopters of papilledema, with many small hemorrhages in the right eye. The visual fields were normal. There was no paralysis of the face or tongue. The tendon reflexes of the upper extremities were normal; those of the lower extremities were more active on the right than on the left. The abdominal and cremasteric reflexes were obtained. There were slight ataxia of the left hand and arm and a suggestion of adiadokokinesis.

Roentgenographic studies revealed calcification in the region of the pineal body. There were an increase in digital markings and separation of the suture lines. Ventriculographic studies revealed the presence of a mass projecting into the posterior part of the third ventricle.

At operation an osteoplastic flap was turned down in the right parieto-occipital area. When the dura was opened close to the superior longitudinal sinus, the hemisphere was retracted laterally and the posterior part of the corpus callosum exposed. An incision was made through this structure, exposing a firm, fibrous tumor, approximately 1.5 cm. in diameter. This was removed piecemeal. Convalescence was comparatively uneventful, but it was then noted for the first time that the eyeballs could not be elevated above the horizontal.

The patient was last examined on April 25, 1936. He was free from symptoms and was working as a painter. The eyeballs could be elevated somewhat above the horizontal, though not as far as normal. The pupils were still fixed to light but reacted promptly in accommodation. The visual fields were entirely normal.

The fact that this patient is free from symptoms seven years after the operation is suggestive evidence that the tumor was completely excised. High voltage roentgen therapy was instituted for one year after the operation, but, as observed by my colleagues and me, therapy as ordinarily given never actually eradicates tumor of the brain. The diagnosis of pinealoma in this case was confirmed by Dr. Louise Eisenhardt.

A case of complete removal of a pineal teratoma has been reported recently by McLean.[7] It was stated that this was the first complete excision of such a tumor. Unfortunately, the patient succumbed a few hours after the operative procedure. In the following case of a somewhat similar pineal teratoma, complete removal was successfully performed by means of the modification of Brunner's [8] approach described by Dandy.[9]

7. McLean, A. J.: Pineal Teratomas, with Report of Case of Operative Removal, Surg., Gynec. & Obst. **61**:523 (Oct.) 1935.

8. Brunner, C., quoted by Rorschach, H.: Zur Pathologie und Operabilität der Tumoren der Zirbeldrüse, Beitr. z. klin. Chir. **83**:451 (Feb.) 1913.

9. Dandy, W. E.: An Operation for the Removal of Pineal Tumors, Surg., Gynec. & Obst. **33**:113 (Aug.) 1921.

CASE 2.—V. R., a boy aged 9 years, was admitted to the University Hospital on March 6, 1935, complaining of headache and vomiting. It was stated that the boy had always been somewhat backward mentally. Except for the usual diseases of childhood, the patient had been well up to the time of the present illness.

The headache and vomiting had commenced six weeks before his admission. The headache involved the frontal region and had gradually increased in severity until it had become continuous. At times the child screamed with pain. The headache apparently was not relieved by change of position. The vomiting had been frequent but was not projectile.

Fig. 1 (case 1).—Photomicrograph of a pinealoma.

A week before his entrance to the hospital the child no longer could walk unaided. Four days prior to admission internal strabismus had developed.

Examination revealed that the boy was acutely ill, somewhat emaciated, drowsy and slow of speech. No abnormal constitutional characteristics were noted. The left eye was kept closed because of diplopia. The head was not enlarged, but Macewen's sign was present. There was slight rigidity of the neck, but the Brudzinski sign was absent. On one occasion marked retroflexion of the head seemed to relieve the headache.

The pupils were unequal, the left being the larger. Reactions to light and in accommodation were sluggish (two and one-half days after instillation of homatropine hydrobromide). There was bilateral palsy of the sixth nerve, more marked on the left. There was incoordination of both horizontal and vertical

movements of the eyes. Upward gaze was not restricted, though the left eye did not elevate quite as well as the right. A few nystagmoid jerks were seen on lateral deviation. Examination of the fundus revealed 2 diopters of papilledema on the right and 3 diopters on the left. No hemorrhages were present. The visual fields were not satisfactory, but there was no suggestion of homonymous hemianopia. The corneal reflexes were present. Hearing was normal. No other palsies of the cranial nerves were found.

There was moderate hypotonia of all extremities. The deep tendon reflexes were equal but slightly diminished. The abdominal reflexes were active. Hoffmann and Babinski signs were not elicited. There was slight ataxia in both hands in the finger to nose test, with a tendency to past pointing. There was ataxia in both lower extremities, more marked than in the hands. Sensory examination gave normal results.

Fig. 2.—Ventriculogram taken in case 2, showing a smooth, round shadow in the posterior part of the third ventricle. The suprapineal recess is still present.

Laboratory studies revealed normal urine and a hemoglobin content of 70 per cent. The Kahn reaction of the blood was negative.

Roentgenographic studies of the head revealed separation of the suture lines, with an increase in the digital markings. There was a faint flaky area of calcification in the region of the pineal body, which was seen only in the lateral projection.

On March 11 oxygen was injected into the ventricles. The fluid was under considerable increase in pressure. The ventriculograms revealed dilatation of both lateral ventricles and the anterior portion of the third ventricle. A smooth, round shadow, almost filling the posterior portion of the third ventricle, was seen just behind the massa intermedia. The suprapineal recess was still present. The diagnosis made was of an encapsulated tumor of the posterior portion of the third ventricle, probably of pineal origin.

While the patient was under anesthesia induced with tribromethanol in amylene hydrate, an osteoplastic flap in the right occipitoparietal area was turned to the midline. The dura was under a moderate increase in pressure. The ventricle

was tapped, giving good relaxation, and the dura was opened. The hemisphere was retracted laterally and the posterior third of the corpus callosum exposed. An incision about 2.5 cm. in length was made through the corpus callosum. The most posterior portion of the splenium was not sectioned. The third ventricle was then entered by opening the tela choroidea. During this procedure an opening was made also into the right lateral ventricle. The upper surface of the smooth-walled encapsulated tumor was seen to be adherent to the veins of Galen. The right small vein of Galen was necessarily clipped. The tumor was slightly

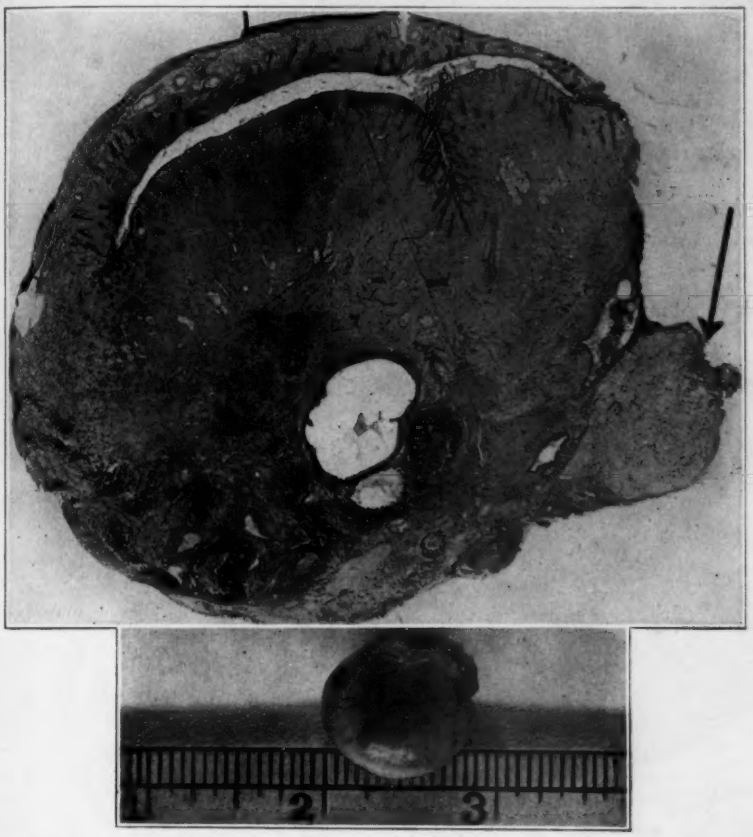

Fig. 3.—Gross specimen and section of the tumor in case 2. The arrow indicates normal tissue of the pineal gland on the pedicle, which is shown in detail in figure 5.

adherent to the thalamus on each side, though chiefly on the left. The pedicle, which was partially calcified, extended posteriorly. The pineal body itself was not seen. The pedicle was sectioned and the entire tumor delivered intact. After careful hemostasis, the usual closure was made without leaving a decompression. Though at no time during the operative procedure was there any marked change in condition, 300 cc. of whole blood was given at the completion of the closure. The patient reacted quickly from the anesthesia.

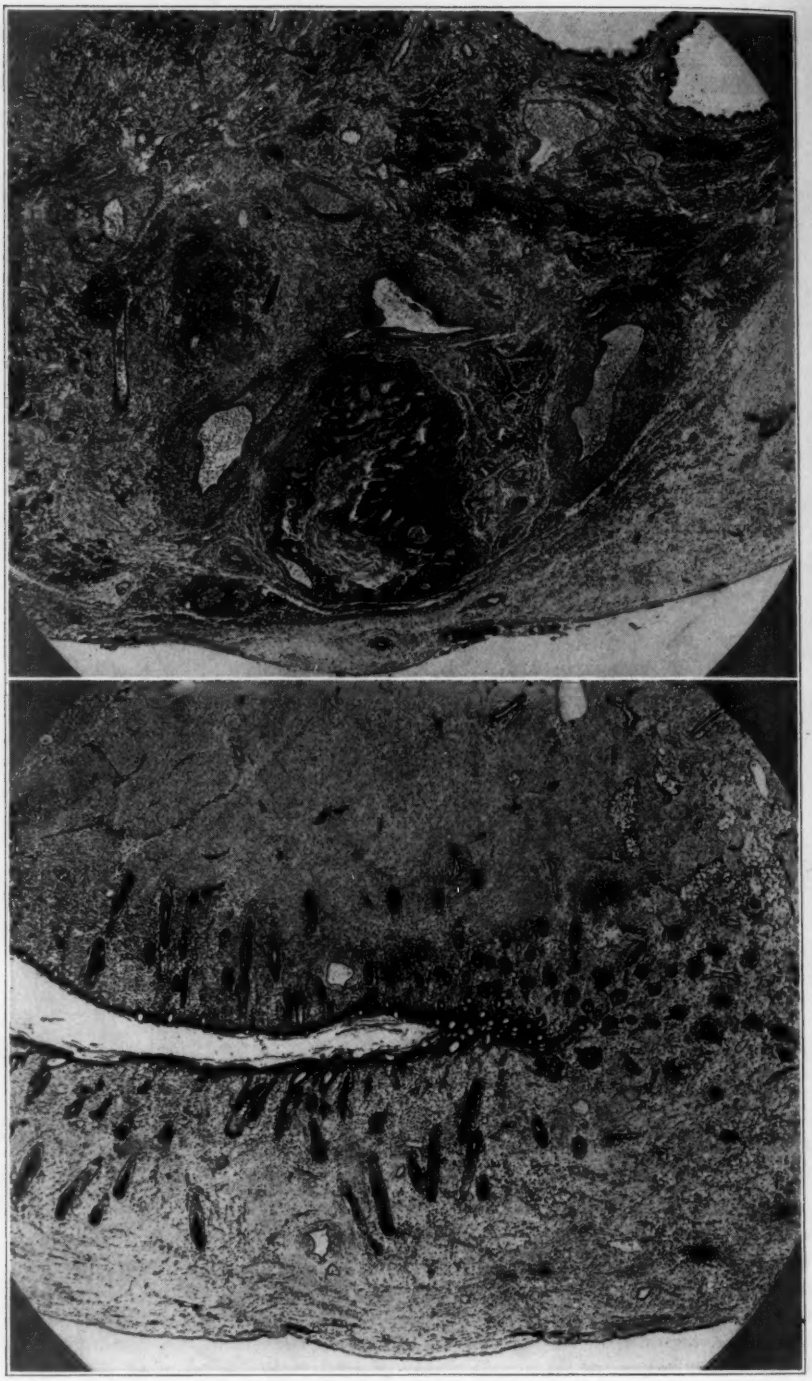

Fig. 4.—Photomicrographs showing structures characteristic of the intestine and accessory parts of the skin.

A description of the tumor by Dr. Carl V. Weller follows:

The operative specimen was a nearly spherical mass, about 2 cm. in diameter. The surface was smooth except for the base of attachment. The mass was elastic when lightly compressed and was pinkish gray. The cut surface was somewhat mucinous, and the mass as a whole appeared moderately gelatinous. Examination of a complete section under a low power microscopic lens showed a crescentic cleft roughly parallel with the surface. This cleft was lined by cornifying, stratified squamous epithelium, with which numerous hairs and sebaceous glands were in relationship. The hair bulbs were embedded in edematous connective tissue, and there were many small pockets of adipose tissue at the same level, which resembled those present in the scalp. At a distance of about 1 cm. from

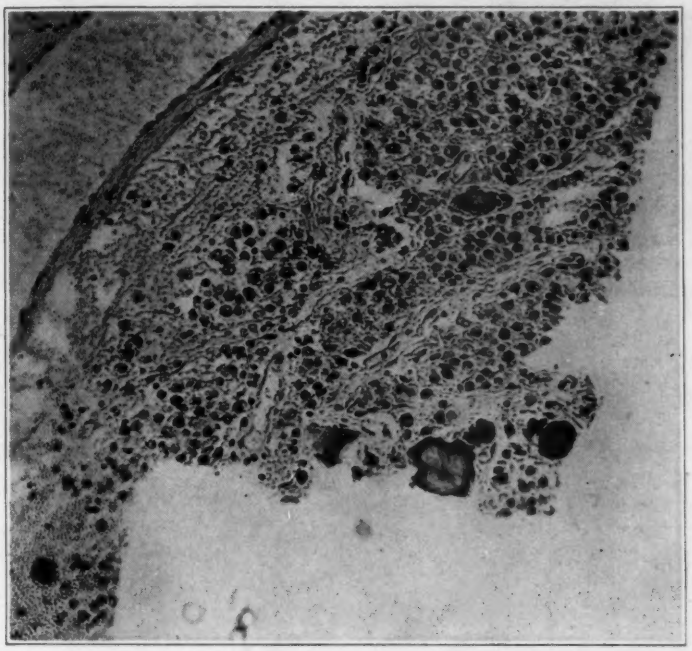

Fig. 5.—Photomicrograph of pineal tissue at the base of the pedicle, indicated by the arrow in figure 3.

this ectodermal complex, in the direction of the area of attachment, there were several small lumens lined by mucin-forming columnar epithelium. Here there were poorly developed crypts of Lieberkühn. Strands of involuntary muscle were observed about this area, and there were solitary lymph follicles in the mucosa. This structure therefore corresponded to the large intestine. The remainder of the mass was composed largely of supporting tissue elements, among which were many small blood vessels in angiomatous complexes. Near the area of attachment was a mass of cartilage, which was partially calcified and largely necrotic. In a small area of the stalk was pineal tissue containing characteristic small calcium concretions. The tumor was therefore a complex trigeminal teratoma, which undoubtedly had arisen from the pineal body.

After operation the patient did not show the drowsiness which is the characteristic result of procedures in the region of the third ventricle. For nine days the rectal temperature ranged from 102 to 103 F., though the wound was healing perfectly. Only on the first postoperative day did the temperature reach 104 F. At this time lumbar puncture was performed, and 90 cc. of blood-tinged fluid was removed. On the tenth day the temperature dropped to 100 F. and from that time it remained normal.

Eleven days after operation the papilledema had receded to less than 1 diopter, and there was improvement in the palsies of the sixth nerve. Eighteen days after

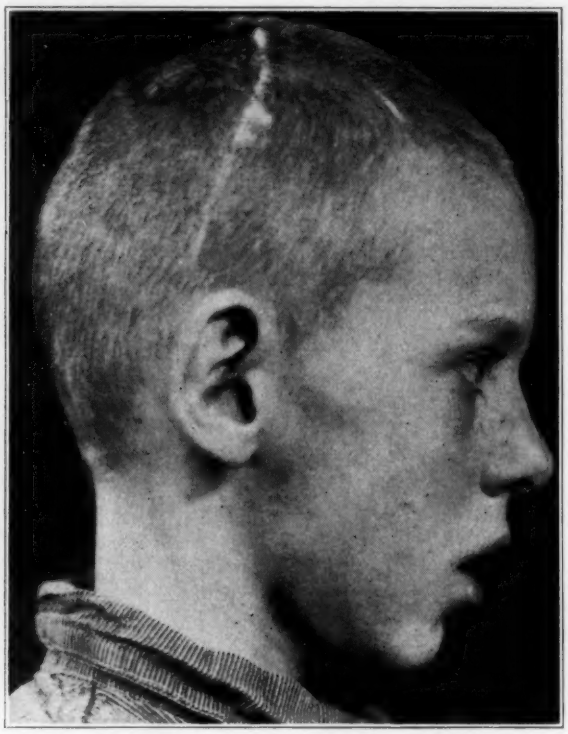

Fig. 6.—Photograph of the patient in case 2, two weeks after operation.

operation the fundi were practically normal. There was only slight weakness in the left sixth nerve. Examination of the visual fields for both form and color then showed complete left homonymous hemianopia with sparing of macular vision.

The patient was again seen one year later. He was still somewhat below par mentally. There were no complaints except occasional diplopia. No palsies of the cranial nerves were present. The fundi were normal, and examination of the visual fields still showed complete left homonymous hemianopia with sparing of the macular area.

COMMENT

We are still unable to account for the complete homonymous hemianopia with sparing of the macular area in case 2. This defect is, of course, characteristic of unilateral resection of the occipital lobe. Harris and Cairns accounted for a similar defect in their case by the fact that they had ligated the internal occipital vein, which drains the greater part of the area striata. I cannot imagine so great a permanent loss of function from mere obstruction of the greater part of the venous return. In case 2 it was believed that we had remained anterior to this vein, though, of course, this could not be stated with certainty.

It is unlikely that division of the posterior part of the corpus callosum has anything to do with the hemianopia. In case 1 no hemianopia developed. Dandy also has had cases in which, after the same procedure we used, no defect in the visual field was found. I am inclined to agree with Dandy that the hemianopia is due to retraction of the cuneus.

TREATMENT

The handling of a pineal tumor is still a debated question. In a large series of radical operations on pineal neoplasm and other tumors of the posterior part of the third ventricle, the operative mortality in our cases has been exceedingly high. Horrax,[10] who has had an extensive experience with these tumors, has adopted a conservative attitude. He advises decompression, followed by roentgen therapy. Only when this fails does he attack the tumor directly. Spurling[11] also has expressed this opinion and has had several remarkable results with this conservative method. He first makes a decompression and follows it with roentgen therapy. If the increased intracranial pressure is not relieved, as evidenced by the size of the hernia following decompression, a transventricular approach is made, and radical removal of the tumor is attempted. The decompression in the meantime has dilated the ventricle on that side, making the approach easier. The pinealoma is somewhat similar in structure to the medulloblastoma and consequently would be expected to respond, at least temporarily, to roentgen therapy.

It must be remembered that in this tumor the obstruction is ordinarily from pressure directly on the aqueduct of Sylvius. Since this channel is only the size of a goose-quill, it is possible that a slight shift in the mass of the brain through decompression might reopen the narrow passage and relieve the obstruction for the time being.

The ventriculogram (fig. 2) is all important in determining the method to be followed. The most valuable position is that described by Peet in 1924—a lateral view of the posterior ventricular system, with the patient face down. This concentrates the air in the posterior part of the lateral and third ventricles and thus best outlines any mass projecting into the posterior part of the third ventricle. We have found

10. Horrax, G.: Further Observations on Tumor of the Pineal Body, Arch. Neurol. & Psychiat. **35**:215 (Feb.) 1936.

11. Spurling, R. G.: Notes on a Conservative Treatment Method of Third Ventricle Tumors, read before the Harvey Cushing Society, Rochester, Minn., May 15, 1936.

this method valuable in differentiating a tumor of the third ventricle from one of the posterior fossa.

Dandy [5] has stated that the suprapineal recess is obliterated in every case of pineal tumor. In case 2 the suprapineal recess was preserved (fig. 2) and we believe that this sign suggests encapsulation of the tumor.

Our opinion as to the procedure to be employed is as follows: If ventricular air studies show that the tumor is smooth walled and round and does not infiltrate one or both thalami, excision should be attempted by an approach through the corpus callosum. If on exposure the tumor is observed to be large, infiltrating and vascular, not even a specimen for biopsy should be taken, since the swelling attendant on such a procedure is likely to result fatally.

If in air studies the tumor appears to be large and invasive, two procedures, to be followed by roentgen therapy, may be tried. The simplest of these is subtemporal decompression. A more radical, but undoubtedly better, procedure is third ventriculostomy—the opening of the distended anterior portion of the third ventricle into the subarachnoid space. This is performed through a subfrontal approach. It has been advocated by Stookey and Scarff [12] in cases of occlusion of the aqueduct of Sylvius and of periaqueductal tumor, and the operation is described in their article. If after these temporizing procedures the increased intracranial pressure persists or recurs at a later date, the tumor must be attacked directly.

SUMMARY

The operative mortality following direct attack on a pineal tumor is still exceedingly high. Two cases are presented in which a tumor of unquestioned pineal origin was successfully removed through the transcallosal route.

The first patient is free from symptoms seven years after operation, and this case is probably the first in which a tumor of undoubted pineal origin was completely removed.

The second case is probably the first in which a teratoma of pineal origin was successfully extirpated.

In neither case was the syndrome of pubertas praecox present.

Excision of a pineal tumor should be attempted if the ventricular air studies suggest encapsulation. Otherwise, decompression or third ventriculostomy or both, to be followed by roentgen therapy, is the procedure of choice.

12. Stookey, B., and Scarff, J. E.: Occlusion of the Aqueduct of Sylvius by Neoplastic and Non-Neoplastic Processes with a Rational Surgical Treatment for Relief of the Resultant Obstructive Hydrocephalus, Bull. Neurol. Inst. New York **5**:348 (Aug.) 1936.

Abstracts from Current Literature

Anatomy and Embryology

THE CENTRAL PATH OF THE LIGHT REFLEX. H. W. MAGOUN and S. W. RANSON, Arch. Ophth. **13**:791 (May) 1935.

The effect of cranial lesions on the light reflex in cats is studied. The lesions were produced by the Horsley-Clarke stereotaxic instrument. Lesions of the caudal part of the optic thalamus, involving only the most rostral portion of the pretectal region, were produced in eighteen cats, which were kept alive from three to five weeks. Bilateral pretectal lesions were made in eight cats, which were kept alive from three to twelve weeks. Unilateral pretectal lesions were made in eight cats, which were kept alive from one to nine weeks. At the close of each operation the nictitating membrane was removed from both eyes, in order to facilitate a study of the size of the pupils. In the case of some cats, two additional operative procedures were performed. Four cats with bilateral lesions and one with a unilateral lesion were subjected to bilateral cervical sympathectomy, with aseptic precautions, from four to twelve weeks after the initial pretectal lesions had been made. After the animals were killed, the extent of the injury to the brain was determined microscopically and was plotted in each case with a standard series of six transverse levels—from the diencephalon, the pretectal region and the superior colliculus of a normal cat's brain. The light reactions were tested by a measure of the width of the pupil, expressed in millimeters, before and during lighting with a fountain pen flash-light.

The authors observed: Lesions in the pretectal region of the cat's brain impair the pupillary light reflex. With bilateral lesions the amount of reduction in the light reflex is roughly proportional to the amount of pretectal destruction. With a unilateral pretectal lesion the light reactions of the contralateral eye are more severely impaired. If the pretectal region is almost completely destroyed on both sides of the brain, with some damage to the rostromedial portion of the superior colliculis, the light reflex is completely and permanently abolished. While minor participation in the light reaction on the part of the rostromedial portion of the superior colliculus cannot, therefore, be excluded, it is clear that at least the greater part of the pupillary light reflex is mediated through the pretectal region.

It should be emphasized that pretectal lesions in cats do not in any sense produce an Argyll Robertson pupil. No observable pupillary reaction to accommodation can be shown in the cat under either normal or experimental conditions. While these lesions cause miosis which lasts a few days, this disappears as the irritation caused by the lesions subsides. In the chronic stage the pupils are widely dilated, owing to obliteration of the pupillary light reflex.

At present it is impossible to say whether miosis in connection with the Argyll Robertson pupil is due to chronic irritation of some part of the pupilloconstrictor path or to associated paralysis of the pupillodilator pathway. Considering the course followed by the pupillary light reflex and by the dilator path descending from the hypothalamus, it is difficult to see how both these could be interrupted by a single lesion of moderate extent. SPAETH, Philadelphia.

THE DISTRIBUTION OF SYMPATHETIC NERVE FIBERS TO THE HIND LIMB OF THE CAT. B. I. BURNS, J. Comp. Neurol. **61**:191 (April) 1935.

This is a study of the distribution of postganglionic sympathetic fibers in the nerves of the hindlimb of the cat and includes the course of these fibers to the blood vessels of that extremity and their behavior within the walls of the blood vessels. The sympathetic fibers were isolated by degeneration of the somatic

fibers to the part. In six cats the nerve trunks of certain spinal nerves were cut between the dorsal root ganglion and the point of entrance of the gray ramus into the nerve. In three cats these were from the fourth lumbar to the third sacral nerve. In the other three cats the third lumbar nerve was included. From nineteen to twenty-two days was allowed for degeneration. Pyridine silver preparations were made of representative nerves and arteries and of the nerve trunks which had been cut in the experiment. Counts were made of the intact sympathetic fibers. In the saphenous nerve about 2,500 sympathetic fibers were counted, and in the nerve to the biceps muscle, over 1,000 fibers. The femoral, saphenous and anterior tibial arteries were studied. In the femoral artery the sympathetic fibers were seen isolated or in very small bundles, and in the saphenous artery and vein, in larger bundles. Between the adventitia and the media a nerve plexus was seen, and within the media these fibers formed a net, although there were occasionally individual fibers or small numbers of fibers. No nerve endings of any type were observed in the adventitia or the media, although encapsulated endings were seen in the perivascular tissues. No nerve fibers were seen in the intima.

ADDISON, Philadelphia.

THE ENDOCRANIAL BLOOD VESSELS OF AMBLYSTOMA TIGRINUM. PAUL GIBBONS ROOFE, J. Comp. Neurol. **61**:257 (April) 1935.

The endocranial blood vessels of Amblystoma tigrinum were studied by serial microscopic sections through the entire head, by microscopic sections variously prepared of the brain with the pial vessels intact, by gross dissection and by direct observation of the circulation in the living animals. Injections of the blood vessels were also made.

The endocranial blood supply is from two sources, the cerebral carotid arteries and the basilar artery. The arterial supply is essentially similar to that of other urodeles. The systemic capillary net in the nerve walls of the brain is relatively simple, with wide meshes. As seen by transillumination, the blood flows rapidly in the arteries and the systemic capillaries and slows abruptly in the larger veins and sinusoids. The thalamus is the richest of all parts of the brain in arterial blood supply, and the olfactory bulbs are next.

All the choroid plexuses are extensively developed. In the fourth ventricle the choroid plexus has both an arterial and a venous supply.

FRASER, Philadelphia.

THE MEMBRANOUS PARTS OF THE BRAIN, MENINGES AND THEIR BLOOD VESSELS IN AMBLYSTOMA. C. JUDSON HERRICK, J. Comp. Neurol. **61**:297 (April) 1935.

This paper is an extension of Roofe's paper by microscopic study of the adult Amblystoma tigrinum. The meninges are intermediate between the meninx primitiva of the lower fishes and the meninges of the frog. Over the spinal cord and most parts of the brain there exists a firm and well defined pachymeninx, closely investing the underlying undifferentiated pia-arachnoid. The dural membrane is lacking over the infundibulum and hypophysis. It penetrates between the choroid plexus of the fourth ventricle and the overlying endolymphatic organs as a loosely organized fibrous tissue, which extends also dorsally to enclose the endolymphatic sacs. The choroid arteries break up into an elaborate capillary bed which pervades the plexuses. A peculiar arrangement of venous sinusoids exists which amounts practically to a double endocranial portal system.

FRASER, Philadelphia.

THE CORTICAL AREA CONCERNED WITH COORDINATED WALKING IN THE RAT. NORMAN R. F. MAIER, J. Comp. Neurol. **61**:395 (April) 1935.

The purpose of this study was to determine whether the destruction of any particular part of the cortical surface of the brain of the rat caused the type of motor incoordination which was observed when rats with a cortical lesion ran

along an elevated pathway 2 inches (5.08 cm.) in width. Animals were trained to run for food over such a pathway. They were then subjected to cortical lesions of various sizes and patterns. A recovery period of from twelve to fifteen days was allowed. The rats were then required to run for food, and the loss in footing and the inability to regain footing were recorded. At the end of periods of observation the rats were killed and the brains removed for histologic examination.

Cortical lesions in the rat do not produce paralysis. The results of this study indicate that coordinated walking in the rat is primarily dependent on a particular cortical region which is structurally partly motor and partly somesthetic. This region lies partly in areas j, f and n of Lashley's modification of Fortuyn's mapping. The first of these areas has been designated as somesthetic and the other two as motor. The region constitutes 5.1 per cent of the cortical surface. It appears to have a coordinating function. No particular part of it seems to be more important than any other. Destruction of tissues surrounding this coordinating region contributes to the disturbances but is not equipotential with the critical region. Destruction of the cortex in the posterior part of the brain does not contribute to the disturbance of coordination in walking. ADDISON, Philadelphia.

PROCESSES OF LOCALIZATION IN DEVELOPING FUNDULUS. JANE M. OPPENHEIMER, J. Exper. Zoöl. **73**:405 (July) 1936.

Vitally stained cleavage blastomeres of the egg of Fundulus heteroclitus were followed to gastrulating stages, and locally stained areas of the gastrulae were traced to their position in the formed embryo. The results were combined to form a tentative scheme of cell lineage. Four of the marginal cells of the sixteen cell stage form the early embryonic shield, which contains endoderm and mesoderm for the region of the head and the first few somites and material for all the nervous system posterior to the forebrain. The outer half of the remaining marginal cells provides material for the germ ring, which contains cells which invaginate to form endoderm and mesoderm for the posterior part of the embryo. The remaining portion of the sixteen cell blastoderm forms extra-embryonic membrane. The greater part of this is transformed into the epithelium of the yolk sac, but some of its cells enter the embryonic shield to form the eye and forebrain. When the presumptive nervous system of the anterior part of the shield is grafted without substrate, it differentiates into developmentally retarded eye and forebrain. If mesoderm is included in the grafts, the eye and forebrain are normally differentiated. Even though the cells which form the eye and forebrain are situated originally outside the shield, the factors responsible for their differentiation are active within the shield. WYMAN, Boston.

CHANGES IN THE LATERAL-LINE ORGANS DURING THE LIFE OF THE NEWT, TRITURUS VIRIDESCENS. ALDEN B. DAWSON, J. Exper. Zoöl. **74**:221 (Oct.) 1936.

The larva of the common newt has functional lateral line sense organs which are superficial and exposed. During the terrestrial red eft stage, the organs partially dedifferentiate, lie deeper in the dermis and are served by an overgrowth of epidermal cells. On resumption of aquatic life the organs again become functional, and communication with the free surface is regained. Maintenance of complete differentiation in this stage appears to depend on the thyroid gland, which in turn is controlled by the anterior lobe of the pituitary. After hypophysectomy and thyroidectomy there is marked regression of all epithelial elements of the sense organ, while stimulation of the anterior lobe of the pituitary results in hypertrophy and hyperplasia of the sensory supporting cells. The cupulae and the cupular secretion are also under endocrine influence. It was previously believed that maintenance of differentiation of the lateral line organs depends largely on the presence of the nerve supply. The present results show a surprising dependence on endocrine factors. WYMAN, Boston.

PRESENCE OF COLLOID INCLUSIONS IN GANGLION CELLS OF THE HUMAN MEDULLA OBLONGATA. GERD PETERS, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:779 (Sept.) 1935.

Peters observed colloid deposits in the ganglion cells of the medulla. These bodies were similar to those described by Scharrer, Gaupp, Divry and others in the cells of the hypothalamic nuclei in man and lower animals. The structures were observed in six of seven cases. In all instances the cells in the hypoglossal nuclei showed colloid droplets. In two cases they were seen in the nucleus funiculi lateralis, the dorsal vagus nucleus and the cells of the reticular substance. The inclusions stained from light red to orange red with the Van Gieson stain, light red with eosin, pale blue with the Nissl technic and yellow brown in Bielschowsky preparations. They did not take the Best stain. They were pale blue with the Alzheimer-Mann stain.

The colloid droplets were present either in small vacuoles at the periphery of the cells or in large vacuoles which sometimes occupied the center of the cells. The cells in which the vacuoles were noted showed no signs of degeneration or other pathologic changes. Empty vacuoles were noted much more rarely in these cases than in the reports of investigations on the hypothalamic nuclei. Another noteworthy difference was the absence of extracellular droplets in these cases.

Peters thinks that more evidence is needed to prove the contention that the presence of colloid bodies within the cells is proof of the secretory activity of ganglion cells. He insists, however, that they are not due to the existence of a degenerative process. They were observed in the intact cells of both young and old persons, as well as in those who died accidentally without preexisting organic disease of any type. The colloid bodies are considered by Peters to be due to passing phases of cellular metabolism.

SAVITSKY, New York.

MICROCEPHALIC FETUS WITHOUT EYES AND NOSE AND WITH SERIOUS DEFECTS OF THE FOREBRAIN, CEREBELLUM, INNER EAR AND ENDOCRINE GLANDS. G. ILBERG, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:1 (Oct.) 1935.

Ilberg reports the case of a 6 month fetus who died immediately after birth. The skull was small (13 cm. long and 4.5 cm. wide). There were no fontanels or sella. The jaw was prognathous and the anus imperforate. The right external ear was poorly developed, there being merely four soft prominences at the site at which the ear should have been. The external auditory canals were not patent. The eyes and nose were absent. Clubfoot was present bilaterally. In the midfrontal region there was a vertical indentation, 2.5 mm. long, from the end of which a somewhat deeper groove extended in a forklike manner 2.5 cm. to the right and to the left, respectively. The cerebrum and cerebellum were absent. No hypophysis was seen. The falx cerebri, tentorium cerebelli, olfactory bulbs and optic and oculomotor nerves were absent. The thyroid, uterus, ovaries, adrenal glands and pancreas were very small. The cochlea was absent bilaterally. Some development of the semicircular canals was seen on the right side. The large olives were both absent. Of all cerebellar structures only the corpus dentatum was observed. The facial nuclei were poorly developed. There was no microscopic evidence of syphilis. Reports of only two similar anomalous fetuses were found in the literature (Raddatz, 1829, and Ahlfed, 1882). Ilberg notes the following facts in the family history of the woman who gave birth to this abnormal fetus: Two siblings had epilepsy in early life; her father and mother were deaf-mutes; the father was alcoholic, sadistic and unquestionably psychopathic, and both grandparents were alcoholic. These factors may play a rôle in accounting for this unusual developmental anomaly.

SAVITSKY, New York.

Physiology and Biochemistry

THE RELATIONSHIP BETWEEN ALCOHOLIC INTOXICATION AND ANOXEMIA. R. A. MCFARLAND and A. L. BARACH, Am. J. M. Sc. **192**:186 (Aug.) 1936.

The present investigation was carried out to determine the extent to which alcohol produces anoxia and that to which the inhalation of from 50 to 60 per cent oxygen and from 0.2 to 10 per cent carbon dioxide counteracts the effects of excess alcohol. Studies were made on the lactic acid and alcohol contents of the blood and on the reactions to psychologic tests. Twenty-three students who did not drink and two students who were addicted to drinking served as subjects. The drinks varied from 0.75 to 1.25 Gm. of ethyl alcohol per kilogram of body weight diluted to a total volume of about 250 cc., or one-third alcohol and two-thirds water and orange juice. It was found that the amount of alcohol in the venous blood showed a decrease while the subject was breathing 50 per cent oxygen and excess carbon dioxide. In five of the twenty-three subjects the decrease was not significant; in a number of instances the decrease was more than 50 per cent. An increase in the lactic acid content of venous blood was observed after the ingestion of alcohol. The pulse and blood pressure also showed a transient rise, followed by a return to the normal or subnormal. There was a general tendency toward improvement in the six psychologic tests after the ingestion of alcohol with a high concentration of oxygen and excess carbon dioxide, as compared to the results with air.

MICHAELS, Boston.

THE CHOLESTEROL CONTENT OF MUSCLE. W. R. BLOOR, J. Biol. Chem. **114**:639, 1936.

Bloor has observed that the three conventional types of muscle show definite differences in cholesterol content. Smooth muscle has the highest content, averaging 0.75 per cent of its dry weight; cardiac muscle the next, with 0.55 per cent, and skeletal muscle the lowest, with about 0.3 per cent. Wide variations in cholesterol content are observed in each type, so that there is considerable overlapping of values. Different skeletal muscles in the same animal have a similar cholesterol content.

The values for the ratio of phosphatide to cholesterol are high (average, 15) for skeletal and cardiac (ventricular) muscle and low (average, 4) for smooth muscle.

The most outstanding differences in behavior between the groups of muscle are: Smooth and cardiac muscle are spontaneously active and have a more varied, and probably quantitatively greater, nerve supply than skeletal muscle; cardiac and skeletal muscle have habitually a much greater expenditure of energy than smooth muscle, and skeletal muscle is not spontaneously active and has the least varied nerve supply. Associated with their spontaneous activity and more extensive nerve mechanism, smooth and cardiac muscle have a much higher cholesterol content than skeletal muscle, while skeletal and cardiac muscle, with their greater production of energy, have a higher phosphatide content.

It is probable that these associations represent, to some extent at least, real functional relations and that cholesterol is related to spontaneous activity of smooth and cardiac muscle and phosphatide to expenditure of energy.

PAGE, New York.

THE QUANTITIES OF PROTEIN LOST BY THE VARIOUS ORGANS AND TISSUES OF THE BODY DURING A FAST. T. ADDIS, L. J. POO and W. LEW, J. Biol. Chem. **115**:111, 1936.

The source of the total protein lost by albino rats during a seven day fast was determined by measurements of the protein content of the various organs and tissues. It was found that the muscles, skin and skeleton contributed 62 per cent of the total amount; the liver, 16 per cent; the alimentary tract, pancreas and

spleen, 14 per cent; the drawn blood, 6 per cent, and the kidneys and heart, 1 and 0.5 per cent, respectively. The remaining 0.5 per cent was derived from other organs. There was no loss of protein from the eyes, the testes and the adrenals. The proportion of the original protein content lost by various organs is widely different. The liver lost 40 per cent of its protein. The prostate and seminal vesicles lost 29 per cent, while the testes and adrenals lost none. The heart, kidneys, drawn blood and alimentary tract lost from 18 to 28 per cent; the muscles, skin and skeleton, 8 per cent, and the brain, 5 per cent. The protection of the brain from loss of essential elements during fasting should be noted.

PAGE, New York.

BLOOD PHOSPHOLIPID AS A TRANSPORT MECHANISM. ROBERT GORDON SINCLAIR, J. Biol. Chem. **115**:211, 1936.

When elaidin is fed to cats, elaidic acid is found in considerable amounts in the phosphatides of the blood plasma within a few hours. If elaidin is fed repeatedly for several days, as high as 37 per cent of the fatty acids in the phosphatides of the plasma consists of elaidic acid. Plasma phosphatide definitely serves as a mechanism for the transport of fatty acids to the tissues, where they are burned. Since no elaidic acid could be detected in the phosphatides of the red cells, except small amounts after several days of repeated feeding of elaidin, it is concluded that the red cells do not participate in the transport of phosphatides.

PAGE, New York.

STUDIES IN HISTOCHEMISTRY: IX. THE QUANTITATIVE DISTRIBUTION OF VITAMIN C IN THE ADRENAL GLAND AT VARIOUS STAGES OF DEVELOPMENT. DAVID GLICK and GERSON R. BISKIND, J. Biol. Chem. **115**:551, 1936.

The quantitative distribution of vitamin C and the number of cells per unit volume in the various regions of the bovine adrenal gland have been determined at developmental stages from the 6 month fetus to the calf. From this the quantity of vitamin C per cell was estimated for the different types of cells present. The fascicular region of the adrenal gland contained the highest concentration of the vitamin at all stages of development. The medulla and the glomerular zone contained concentrations of the same order of magnitude. The concentration increased in all regions with the development of the gland, reaching a maximum in the calf and falling off in the adult animal. Both the size of the cells and the quantity of vitamin per cell increased regularly from the fetal to the adult stage of the animal.

PAGE, New York.

THE SUPERFICIAL ABDOMINAL REFLEXES. E. FRETSON SKINNER, J. Ment. Sc. **82**:394 (July) 1936.

In contrast to the cremasteric reflex, the abdominal reflexes are absent in infancy and develop only in childhood. Their late ontogenetic appearance suggests a more recent phylogenetic development. The abdominal reflexes appear at the same time as the Babinski reflex and obviously depend on the maturity of the pyramidal tracts, especially the direct tracts. These pathways are probably connected with the development of erect posture in man.

In quadrupedal animals the anterior abdominal wall is not subject to direct attack. With the assumption of erect posture, the abdomen becomes open to direct assault, hence the evolution and development of a quick reflex contraction as a method of defense. This is the reason that the abdominal reflexes are absent in domestic animals and that their earliest appearance is in primates. The primates have abdominal reflexes identical to those of man. Fear may also cause abdominal contraction.

The abdominal reflexes are absent in: (1) infancy, up to the seventh month of life; (2) sleep and surgical anesthesia; (3) cerebral diseases of various kinds,

and (4) violent emotion, especially fear. In infancy and under the conditions enumerated one deals with the reaction of the nervous system found in primitive man, without fine differentiation; hence the absence of the more highly differentiated local reflexes. Absence of these reflexes is a release phenomenon. On the other hand, absence of reflexes can also be explained on the basis of the underdevelopment of the pyramidal tracts or of anything which interferes with the function of these tracts.

The extreme promptness of the abdominal reflexes leads Skinner to believe that they are a neuronic discharge by a neuron which was previously charged, so that the stimulus to the segmental spinal arc is merely a trigger which explodes a mine already laid.

KASANIN, Chicago.

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CHEMICAL TRANSMISSION OF EXCITATION FROM MOTOR NERVE TO VOLUNTARY MUSCLE. G. L. BROWN, H. H. DALE and W. FELDBERG, J. Physiol. **87**:42P (July) 1936.

If acetylcholine is suddenly injected at close range directly into the artery supplying a muscle, such as the cat's gastrocnemius muscle, during temporary arrest of the circulation, a very small dose, in from 0.25 to 0.5 cc., regularly produces a contraction of the muscle not much less rapid than a maximal motor nerve twitch, and of equal or greater tension. Contractions of such dimensions have been obtained with doses of from 2.5 to 10 micrograms in different experiments. With a larger dose, such as 20 micrograms, a quick contraction of as much as 6 Kg. tension is obtained from a muscle giving a maximum motor nerve twitch of 2 Kg. The apparent insensitiveness of normal mammalian muscle to acetylcholine, hitherto an objection to the function of the substance as a chemical transmitter, disappears when access is sufficiently rapid.

If physostigmine (from 0.2 to 0.3 mg. per kilogram of body weight) is given intravenously to a spinal cat, the tension of a gastrocnemius twitch in response to a single maximal motor nerve volley quickly increases by as much as 130 per cent. Electrical records show that the potentiation is due to repetitive response of the muscle, with a rhythm of about 100 per second. Physostigmine has no such effect on the response of denervated or fully curarized muscle to direct stimulation.

ALPERS, Philadelphia.

THE EFFECTS OF DRUGS ON TRANSMISSION FROM NERVE TO VOLUNTARY MUSCLE AND ACCOMMODATION TO DIFFERENT RATES OF DESTRUCTION OF THE CHEMICAL TRANSMITTER. S. L. COWAN, J. Physiol. **87**:43P (July) 1936.

It was found previously (Cowan, 1936) that when the nerve to the frog's sartorius muscle was stimulated at 150 per second, the Wedensky inhibition at the nerve ending soon developed but that, when stimulation was continued after the maximum inhibition, tension rose again slowly, remained steady for several seconds and then declined slowly. After from 20 to 100 micrograms of prostigmin (the dimethylcarbamic ester of 3-oxyphenyltrimethylammonium methylsulfate) had been added to the bath (50 cc.), inhibition occurred earlier and was deeper, and recovery was slower. Larger doses of prostigmin deepened the inhibition so much that often the preparation responded with only a single twitch. These and other results suggested that the Wedensky inhibition is due to local accumulation of undestroyed acetylcholine. This conclusion has been modified by further experiments.

To eliminate a possible curare-like action of prostigmin, the dimethylcarbamic ester of 3-hydroxyphenylmethyldiethylammonium iodide was used. Preparations which had been treated with this substance gave myograms which were practically identical, except for superimposed small fibrillations, to those which had been given by preparations treated with equivalent amounts of prostigmin.

The nature of the deepening of the Wedensky inhibition at the nerve ending has been examined by the methods of Lucas (1911) Adrian and Lucas (1912) and

Adrian (1913). Lucas found that for the production of a summated contraction in a nerve-muscle preparation the minimal interval between two stimuli is longer than the absolutely refractory period of the nerve by about 20 per cent and that for the production of the Wedensky inhibition the second stimulus has to fall within the 20 per cent interval. This observation was confirmed and it was found that prostigmin greatly increased the minimal interval, even beyond the time in which summation is possible (long minimal interval), without changing the refractory periods of the nerve or muscle (Cowan, 1936). In heavily poisoned preparations, the long minimal interval sometimes reached from 20 to 30 seconds, or if two stimuli separated by from 4 to 8 milliseconds were applied to the nerve, their depressant effect persisted for more than 0.5 minute. This long-continued effect could be prevented by atropine.

It is insufficient merely to suppose that the Wedensky inhibition occurs when the concentration of acetylcholine exceeds the threshold necessary for stimulation and reaches an inhibitory concentration. If this were true, a twitch ought to occur at the close of inhibition, when the acetylcholine concentration sinks from an "inhibiting" to a "stimulating" level. Further experiments suggest that just as two conditions, the threshold and the rate of change of the current, govern excitation by electric currents, so is excitation by acetylcholine dependent on a local threshold concentration and the rate of destruction of the chemical transmitter.

ALPERS, Philadelphia.

THE SPREAD OF ACTIVITY IN THE CEREBRAL CORTEX. E. D. ADRIAN, J. Physiol. **88**:127, 1936.

With three Matthews oscillographs fed through amplifiers from leads on the surface of the cortex, synchronous records were obtained of cortical potentials at various distances from a unipolar stimulating electrode. The rabbits, cats and monkeys employed were usually anesthetized with dial. Weak stimuli gave a local potential lasting 0.01 second, during which the stimulated point remained negative to points 3 mm. away, which in turn were positive to more distant points. A stronger stimulus induced a large wave of positivity. With repetitive stimulation this wave spread slowly in a circle, often for 8 but rarely for 10.5 mm. It showed facilitation and after-discharge. When it arose in the motor cortex, it was associated with the movements represented at its site, and its after-discharge was synchronized with clonic after-discharge of muscles. The potentials are believed to occur in cells rather than in fibers.

MCCOUCH, Philadelphia.

RESULTS OF RECENT STUDIES IN THE FIELD OF THE NEURON THEORY. E. NIESSL VON MAYENDORF, Monatschr. f. Psychiat. u. Neurol. **93**:245 (July) 1936.

The neuron theory is closely associated with certain pathologic observations, one of which is the well known rule that after destruction of a nerve cell its axon disintegrates and after injury to the axon the part cut off from the cell body undergoes secondary degeneration. By tracing the secondary degeneration, the direction in which nerve impulses travel has been determined. Thus, the cells giving rise to sensory fibers have been localized peripherally and those giving rise to motor fibers have been located in the cerebral cortex. Apparently inconsistent with these observations is the fact that old foci of softening in cortical sensory areas are usually associated with descending degeneration of the affected sensory tracts and their subcortical neurons. This may mean merely that the cortical end-stations of sensory fibers are trophic centers for these fibers. The large pyramidal cells encountered in the cortical sensory areas may perhaps be sensory neurons from which sensory tracts originate. These large cells regularly become shrunken after destruction of sensory tracts. Furthermore, they possess many widely branching processes, which come into close contact with numerous small neurons. Such an arrangement would bring afferent impulses into relation with definite groups of small cortical nerve cells, thereby forming the substratum of an exactly determined localization of function.

According to the neuron theory, wallerian degeneration is confined to the involved axons and does not spread from one neural element to another. However, von Mayendorf has observed three cases in which the pathologic changes failed to conform to this rule. In each case the brain showed an area of softening involving the cortical visual region. Secondary degeneration of the optic radiation was traced from the focus of softening to the lateral geniculate body, which showed partial or complete loss of cells with wallerian degeneration of corresponding parts of the optic tract and optic chiasm. As a result of these observations, von Mayendorf comes to the following conclusions: (1) Cellulifugal degeneration occurs when cortical sensory neurons are damaged, suggesting that they conduct cellulipetal impulses; (2) the trophic and functional nerve unit is not the neuron but the conducting neuronal columns, elements of which may well be in continuity with one another, thereby assuring the exact reproduction of peripheral stimuli in the cortical sensory areas.

ROTHSCHILD, Foxborough, Mass.

Neuropathology

TUMORS OF THE CHOROID PLEXUS IN CHILDHOOD. J. H. FRIEDMAN and C. I. SOLOMON, Am. J. Dis. Child. **52**:114 (July) 1936.

Friedman and Solomon review the literature on thirty-four reported cases of papilloma of the choroid plexus in adults and children and add a case of their own. The review disclosed that in the great majority of cases the presence of a tumor of the brain was not recognized and that in the cases in which it was recognized a correct diagnosis of the location of the lesion was not made. Of the thirty-five cases reported, including that of the authors, papilloma of the choroid plexus occurred in the left lateral ventricle in eleven, in the right lateral ventricle in three, in the third ventricle in six and in the fourth ventricle in fifteen. Fourteen patients were under 15 years of age; six, between 20 and 40, and seven, between 40 and 60. The case described was that of a boy aged 20 months in whom there developed progressive right hemiparesis with increased tonus, hyperactive deep reflexes on the right, absence of abdominal reflexes on the right, a Babinski sign bilaterally, blurring of the nasal margins of the disks and engorgement of the retinal veins. The head measured 21 inches (53.3 cm.) in circumference. An encephalogram showed encroachment of a mass on the left lateral ventricle and displacement of the ventricles to the right. The child died before operation. Autopsy showed a tumor of the left lateral ventricle, measuring 7.5 by 6 cm., with the histologic appearance of papilloma of the choroid plexus.

Study of the pathologic appearance and pathogenesis of this tumor indicates: It may arise from the choroid plexus of any ventricle; it is circumscribed, though not encapsulated, and varies in size; it may be solid or cystic, as the result of secretory activity of the tumor cells, and is predominately benign, although it may become invasive or metastatic, and it may produce "neighborhood symptoms" or become obstructive. The characteristic histologic appearance is that of villi, with a central core of connective tissue rich in blood vessels. The villi are lined with cuboidal or tall columnar epithelial cells arranged in a single layer, resembling normal choroid plexus. Glia cells are absent.

The important clinical sign in infants is progressive enlargement of the head due to obstructive hydrocephalus. Other tumors causing obstructive hydrocephalus are midcerebellar glioma, ependymoma, pineoblastoma, abscess and tuberculoma. In these instances the enlargement is not present at birth but occurs in infancy, thus differing from obstructive hydrocephalus due to congenital stricture of the aqueduct of Sylvius, which is present at birth. Communicating hydrocephalus secondary to processes obstructing the flow of cerebrospinal fluid outside the ventricular system is most frequently on an inflammatory or a traumatic basis. Friedman and Solomon emphasize the importance of ventriculography in differentiating the causes of enlargement of the head.

WAGGONER, Ann Arbor, Mich.

EXTENSIVE PIGMENTED NEVUS ASSOCIATED WITH PRIMARY MELANOBLASTOSIS OF LEPTOMENINGES OF BRAIN AND SPINAL CORD. E. W. NETHERTON, Arch. Dermat. & Syph. **33**:238 (Feb.) 1936.

The similar ectodermal origin of the skin and the nervous tissue suggests that both may suffer developmental anomalies from common or analogous developmental defects. The occasional association of mental deficiency and neurofibromatosis is cited as an instance. Melanoma of the meninges, however, is usually of metastatic rather than of developmental origin; a case illustrating the rare coincidence of primary melanoblastosis of the meninges and a pigmented nevus is presented. A youth aged 17 complained of headache, blurred vision, vomiting and defects of memory. He had 4 or 5 diopters of swelling, a large hairy nevus over the face, neck and scalp and smaller nevi over the body. Two operations were performed: suboccipital craniectomy—which revealed a bluish gray mantle over the posterior surface of the medulla, resembling a venous angioma—and cervical laminectomy. The latter revealed that the cord was completely covered by a bluish gray sheath, which at autopsy was seen to be a cylinder of tumor tissue replacing the pia-arachnoid. The cells of this mass had oval, vesicular nuclei; scattered throughout them were numerous, irregular elements containing coarsely granular, yellowish brown pigment. Mitosis was infrequent. The pia of the medulla was similarly involved. The whole picture indicated diffuse melanoblastosis of these meninges.

The superficial portion of the nevus consisted of cells containing inadequate quantities of protoplasm and chromatin, while all through the mass were large multinucleated cells and others containing coarsely granular pigment. The picture was that of the "giant neuronevus of the scalp" described by Masson. In discussing the relationship of the nevus to the meningeal anomaly, Netherton suggests three possibilities: (1) that the meningeal melanoma is metastatic, (2) that the two sets of tumors are unrelated and exist only by coincidence and (3) that they are both the product of widespread ectodermal developmental disturbance. The last explanation appears to be the most reasonable, and Netherton suggests that a lesion of this type may be considered as filling the gap between extensive benign melanoma of the skin and primary melanotic tumor of the meninges.

DAVIDSON, Newark, N. J.

ÉTAT MARBRÉ. A. MEYER and L. C. COOK, J. Neurol. & Psychopath. **16**:341 (April) 1936.

Two cases of état marbré (status marmoratus) are reported in which characteristic clinical and anatomic observations were made. In the first case, beside localization of the état marbré in the striate body, nonhypermyelinated glial scars were present in the external capsule, globus pallidus, substantia nigra, subependymal regions, dentate nucleus and olivary bodies. There was some demyelinization of the white matter of the cerebellum and cerebrum. In the second case the état marbré was present only in the thalamus, but other regions showed the changes noted in the first case. Because of these widespread changes, Meyer and Cook criticize the conception of état marbré as a clinicopathologic entity. The presence in the reticulate zone of the substantia nigra of the pigment described by Hallervorden and Spatz and the involvement of the dentate nucleus suggest a relationship of état marbré to conditions such as Hallervorden-Spatz disease *(état dysmyélinisé)* and disturbances of the dentate-rubral system. Meyer and Cook stress the importance of birth trauma as an etiologic factor. They agree, however, that the etiology of this condition is probably not uniform, although the same pathophysiologic mechanism may be responsible. They stress the need for further investigation of the mechanisms of hypermyelinization, retiform arrangement of the scars and their predilective site.

N. MALAMUD, Ann Arbor, Mich.

CONTRIBUTION TO THE STUDY OF DIFFUSE CEREBRAL SCLEROSIS. ROLAND PFISTER, Arch. f. Psychiat. **105**:1 (May) 1936.

Pfister reports two cases of diffuse cerebral sclerosis in which clinical and histologic studies were made. The patient in case 1 belonged to a family two members of which were previously reported on by Scholz (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **90**:5, 1925; **147**:389, 1933). In this case the clinical and pathologic observations were similar to those described by Scholz. There was slowly developing, progressive spastic tetraplegia, accompanied by brown discoloration of the skin. The changes in the skin were first noticed at the age of 3 years and became progressively more marked. The neurologic disturbances began at the age of 7 years, and the patient died at the age of 8½. Pathologic examination revealed marked bilateral atrophy of the adrenal glands. In the brain there were large areas of recent and old degeneration of the medullary sheaths and, to a less pronounced extent, destruction of the axis-cylinders. These were replaced to some extent by neuroglial tissue. In case 2 no familial tendencies were shown, but otherwise the clinical and histologic observations were much like those in case 1. In case 2, however, there was no opportunity to make a complete autopsy; therefore the adrenals were not studied.

The presence of the brown discolorations of the skin in both cases and the pathologic condition of the adrenals in case 1 indicate some relationship between this disease and endocrine disturbances.

MALAMUD, Iowa City.

ANATOMIC-HISTOLOGIC STUDIES IN CASES OF MANIC-DEPRESSIVE PSYCHOSIS. F. MEYER, Monatschr. f. Psychiat. u. Neurol. **91**:137 (June) 1935.

Meyer reports the results of detailed histologic study in four cases of manic-depressive psychosis. The first case was that of a man aged 60, in whom a manic attack was followed by sudden stupor and death. The lungs showed bronchopneumonia. There was thickening of the pia-arachnoid, which displayed many fibroblasts and macrophages and a few multinucleated giant cells. In some places many red cells were strewn through the leptomeninges. In the cortex of the frontal, temporal and occipital lobes there was diffuse paucity of nerve cells, especially in the third layer, and small acellular areas were observed. The second case was that of a man aged 38, who died of bronchopneumonia seventeen days after the onset of a severe manic attack. The pia-arachnoid was edematous and greatly thickened, showing numerous macrophages and multinucleated giant cells with marked proliferation of fibrillary elements, which frequently took the form of tuftlike excrescences. There were a small area of softening in the cerebellum and a recent extravasation of blood in the region of the locus caeruleus. Thickening and hyalinization of the media were noted in the arteries of all organs. The thyroid was enlarged, and the kidneys exhibited small foci of proliferated connective tissue with round cell infiltration. The third case was that of a man aged 62, who had a manic attack lasting several months, followed by severe depressive stupor with rapid circulatory failure and death. In this case the pia-arachnoid was thickened and edematous and in some places rich in cells. The pineal gland was cystic. The endothelial cells of the liver, spleen, adrenal glands and pars anterior of the pituitary gland were swollen, often lying in the lumen of the capillaries. There was marked increase of connective tissue in the thyroid gland, and the testes presented the picture of widespread fibrous orchitis. The fourth case was that of a man aged 44, who while recovering from a depressive attack, died suddenly after eating a quantity of fruit and drinking a large amount of water. In this case the stomach and the upper portion of the small intestine were greatly dilated. The spleen was enlarged, and there were subepicardial and subpleural hemorrhages. The thyroid gland showed a great increase of connective tissue. The endothelial cells of the liver, spleen and cortex of the adrenal glands gave indications of activation. A small acellular area was observed in the cortex of the temporal lobe. In the choroid plexus many of the vessels were thickened, and there was hyaline degeneration of many of the villi.

In discussing these cases, Meyer noted that the changes in the internal organs were scant as compared with those he had observed in cases of schizophrenia. Most of the alterations pointed to an unknown toxic process. The observations in the last two cases particularly suggest that endocrine dysfunction may play a rôle in manic-depressive psychosis. However, no conclusion is reached on the question whether the changes bore any etiologic or pathogenetic relation to the mental illness.

ROTHSCHILD, Foxborough, Mass.

GLIOMAS. H. J. SCHERER, Virchows Arch. f. path. Anat. **294**:790, 795 and 823, 1935.

In the first of three articles, which constitute the opening contributions to a promised thorough investigation of gliomas, Scherer criticizes the current cytologic and histologic trends in the study of this group of tumors as being limited too narrowly to consideration of the tumor cells. He insists that the tumor cell does not exist—that there is no specific tumor cell with characteristics that distinguish it from the normal cell. He maintains that a tumor is a dynamic whole or organization or organism, the constituents of which react to and on each other, and that the tumor as a whole reacts to its environment, just as the host reacts to the tumor and to his environment. The phenomena of the growth, structure and reactive processes of the tumor as a whole are more important than the morphologic character of the tumor cells. It is from this standpoint that he proposes to investigate gliomas. For his purpose he has used not operative but necropsy material in which the tumor could be studied in its entirety and in relation to the brain. Sections of the entire neoplasm stained by the Nissl method have been employed. Other neurohistologic methods have been used, as indicated.

The second contribution, the title of which may be translated "Limitations of Cytodiagnosis of Tumor of the Brain," is a more specific critique of current methods, based on the study of two neoplasms termed "glioblastoma multiforme ganglioides." The tumors contained mononucleated and multinucleated giant cells of a type usually interpreted as immature and atypical ganglion cells. Tumors of this type have been described in the recent literature under the names "ganglioneuroma," ganglioglioma," "astroblastoglioma," retothelsarcoma" and others. The giant cells have none of the essential characters of ganglion cells and are not ganglion cells. He severely criticizes the designations "spongioblastoma" and "glioblastoma multiforme" as representing a hodgepodge of neoplasms that have in common only such morphologic immaturity and pleomorphism of their cells that the origin of the cells cannot be determined.

In the third and longest contribution, entitled "Angioblastic Glioma," Scherer leaves the field of polemics and proceeds to observations of his own. He describes in detail the histologic features of, and discusses the significance of, peculiar vascular structures in glioma. These have been previously described, but, he thinks, their significance has not been recognized. The structures are of two types. One type consists of a localized group of capillary and precapillary vessels formed by the intimal or adventitial capillarization of a restricted portion of a larger vessel. The other type is glomerulus like. It consists of a convoluted capillary vessel with proliferated endothelium. In many of the structures can be recognized an afferent and an efferent vessel, by means of which they are united to an arteriole. These structures have the following situations: about areas of necrosis, where they are polarized toward the necrosis; in non-necrotic tumor tissue, and in the advancing margin of the tumor, where they are directed toward the tumor and where they can be differentiated from dilated preexisting vessels. They may undergo fibrosis and lead to the formation of fibrous nodules. In the tumor tissue they may be covered by tumor cells, which here reveal greater growth activity than in other parts of the tumor. The glomerular vessel and its covering mass of tumor cells form a fairly sharply circumscribed cellular nodule. The structures described occur in groups in localized areas. The evident equal age of the structures in a group indicates their sudden and eruptive formation as a reaction to local growth stimuli. They were seen most often in two types of

glioma, although in smaller number they have been seen in other types variously named in the current classifications. Of the two predominating types, one is a large infiltration tumor arising in the white matter of the cerebrum. This tumor is histologically and clinically highly malignant; it is cellular and pleomorphic. The other type is smaller and more sharply circumscribed and arises in the white matter of the cerebrum or brain stem. Tumors of the same cellular morphologic structure as these two groups may reveal more of the vascular structures. The vascular complexes cannot be and are not used as a criterion in classifying gliomas. There is no characteristic angioblastic glioma. The term is used in a purely descriptive manner to cover structures that may arise in any form of growing glioma and that are the expression of biologic phenomena in restricted areas of the tumor.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

THE CENTRAL NERVOUS SYSTEM IN ACUTE METALLIC POISONING. A. ESSER, Deutsche Ztschr. f. d. ges. gerichtl. Med. **25**:239, 1936.

Much information is packed into tables in this article, which deals with metallic poisoning in the spinal cord, medulla, brain stem and cerebrum. The effects of strontium, barium, magnesium, aluminum, thorium, thallium, zinc, cadmium and mercury were studied. Dosages are recorded in instances of ingestion of these substances by accident or with suicidal intent. In the spectrographic investigations Esser employed condenser currents, the electric spark and high frequency methods.

RUKSTINAT, Chicago. [ARCH. PATH.]

EXTRAMEDULLARY PIAL LIPOMAS ALONG THE POSTERIOR ROOTS. EUGEN SCHERER, Ztschr. f. d. ges. Neurol. u. Psychiat. **154**:507 (Jan.) 1936.

Scherer reports the case of a woman aged 42, in whom signs of compression of the spinal cord developed one and one-half years before death. The illness began with spastic paraparesis, which was more marked on the right. Sensory changes were first noted on the right side of the chest and the right upper limb. Finally, complete paralysis of both lower limbs appeared, with weakness of the right upper limb and a sensory level in the midcervical region. Paralysis of the sphincters was also present. A roentgenogram of the spine revealed normal structure. Autopsy showed evidence of sepsis, with the portal of entry in infected decubital ulcers. The spinal dura was tense throughout. Within the dura was a yellowish tumor, lying dorsolaterally over the cord on the right side and extending from the level of the junction of the fourth and fifth cervical segments to the fifth dorsal segment. The tumor was shaped like a flattened spindle, with its wider end cephalad. It measured 2.7 cm. at the widest point, at the level of the cervical swelling, and 14 cm. in length. The cord was pushed anteriorly and to the left by the lipoma. The dura was adherent to the surface of the tumor but was easily separated from it. The tumor was enveloped in a delicate capsule of connective tissue. A few longitudinal vessels were present on the surface of the tumor. The pial vessels extended directly into the capsule at the distal end of the mass. There was no spina bifida. Deposits of fatty tissue were observed in the bodies of the lower cervical and upper dorsal vertebrae, especially the second dorsal and the sixth and seventh cervical. The dorsal roots all passed directly through the lipoma on the right side, separating fanwise within the tumor before entering the cord.

Microscopic study of the tumor confirmed the diagnosis of lipoma. There was little connective tissue. The fatty tissue was not lobulated. There was proliferation of the intima of the vessels passing through the tumor. The perineural connective tissue of the nerve roots within the tumor was increased. There was little change in the endoneural connective tissue. The cord was compressed, with demyelinization of the long tracts and atrophy of the ganglion cells in the posterior and anterior horns on the right side. The dentate ligaments were pushed dorsally by the tumor tissue and were attached directly to the fibrous capsule about the tumor.

The origin of the tumor was from the pia mater. It was also clear that the site of origin of this tumor was the region of the posterior roots. Similar extra-

medullary pial lipomas along the dorsolateral aspect of the cord and arising from the region of the posterior roots have been reported by Braubach (*Arch. f. Psychiat.* **15**:489, 1884), Ritter (*Deutsche Ztschr. f. Chir.* **152**:189, 1920) and Stookey (Intradural Spinal Lipoma, ARCH. NEUROL. & PSYCHIAT. **18**:16 [July] 1927). The tumor arises from the perivascular tissue of the pia mater.

SAVITSKY, New York.

HISTOLOGIC CHANGES IN INSULIN CONVULSIONS. N. TANI, Psychiat. et neurol. jap. **39**:5 (Aug.) 1935.

Rabbits were given subcutaneous injections of from 1 to 10 units of insulin per kilogram of body weight. This was repeated from four to eight times in most cases, and in a few, as many as from forty to eighty times. Convulsions, tremor, ataxia and pupillary disturbances developed. The brain showed diffuse changes in the ganglion cells and generalized glial hyperplasia. These lesions were especially marked in the corpus mamillare and the inferior olive. The changes are attributed to a functional disturbance in circulation characterized by loss of the capacity of the cerebral vessels to contract, as a result of repeated dilatation from the convulsions.

ALPERS, Philadelphia.

HISTOLOGIC CHANGES IN THE HYPOTHALAMUS, SUBSTANTIA NIGRA AND INFERIOR OLIVE IN EPILEPSY. N. TANI, Psychiat. et neurol. jap. **39**:9 (Sept.) 1935.

The hypothalamus and inferior olive were studied intensively in fifteen cases of epilepsy. In the hypothalamus severe changes in and loss of ganglion cells were observed in the majority of cases. In one case there was softening in the corpora mamillaria. In the zona reticulata of the substantia nigra were fatty changes in and loss of cells and progressive changes in the glia. In the zona compacta there was often depigmentation of the cells, with gathering of the pigment around the vessels. Severe degenerative changes were observed in the cells of the inferior olive.

The severity of these changes appears to be parallel with the severity of the clinical picture, as judged by the number and severity of the convulsions.

ALPERS, Philadelphia.

Psychiatry and Psychopathology

ARE ATTITUDES BIOLOGICAL OR CULTURAL IN ORIGIN? G. W. ALLPORT and R. L. SCHANCK, Character & Personality **4**:195 (March) 1936.

In order to shed new light on the origin of attitudes, the following exercise was given to students in social psychology at Harvard University and Radcliffe College annually for five years: "In greater or less degree the law condones the taking of a human life under the following circumstances. Assuming that the circumstances of the combat always give fair play to both combatants, arrange these situations in the order of greatest justification for the killing at the top of the list to least justification at the bottom, following your own feelings as a guide.

(a) in defending the safety of one's family
(b) in protecting one's property against trespassers
(c) in defending the honorable reputation of a member of one's family
(d) in defending one's property against burglars
(e) in defense of one's own life
(f) in fighting for one's country
(g) in order to protect one's own honor or reputation
(h) in order to save the life of another human being."

In respect to all but three of these situations, the order of rank of justifiability for homicide remained the same year after year. Only in the group of situations

dealing with "honor" was there any shifting. In no instance did honor rise as high in the scale as defense of persons, and in no case did it fall as low as defense of property. "The unambiguous decision of our subjects is that an immediate threat to one's physical safety is by far the most justifiable cause of homicide." No answer seems possible to the authors without reference to the instinctive nature of the struggle response. The more primitive the situation in the biologic sense, the more intense and the less variable is the attitude. Cultural influences are demonstrated within this basic biologic limitation. Owing either to civilized codes or to the traditional "magic" associated with one's name and reputation, situations involving honor take precedence over situations in which property is an issue. Furthermore, the minor variability of the justification from the point of view of differences based on sex, groups and time demonstrates the operation of selective cultural influence.

"The origin of attitudes, in a functional sense, then, is always biological. The model upon which they are fashioned is often, though not always, cultural."

HARPER, Philadelphia.

THE PROBLEM OF LONG-CONTINUED, LOW GRADE FEVER. HOBART A. REIMANN, J. A. M. A. **107**:1089 (Oct. 3) 1936.

Reimann reports on a study made on a group of sixteen women whose oral temperature reached levels slightly higher than 37 C. (98.6 F.) for years, to determine whether or not infection or other organic disease was present to cause the fever. Five of those examined were apparently normal healthy women, but the rest were regarded as neurotic. The temperature in each case reached levels over 37 C. (98.6 F.) daily for months or years but seldom exceeded 37.8 C. (100 F.) unless actual infection or other known causes intervened. Complete physical examination, long and repeated observation, roentgenographic studies and laboratory and biologic tests failed to reveal an underlying cause for the hyperthermia. It was concluded that a certain proportion of normal persons have temperatures regulated at levels slightly higher than 37 C. (98.6 F.) and that a temperature at these levels is often found in neurotic persons.

EDITOR'S ABSTRACT.

RELATION OF PERSECUTORY DELUSIONS TO THE FUNCTIONING OF THE GASTRO-INTESTINAL TRACT. FRANZ ALEXANDER and W. C. MENNINGER, J. Nerv. & Ment. Dis. **84**:541 (Nov.) 1936.

Pessimism, fear of being unable to earn a living and belief that one is not loved are, according to Alexander, characteristic of "anal character" and are found in many patients with psychogenic chronic constipation. The same defeatist attitude in exaggerated form is common in melancholia, along with the tendency to deny all obligations toward the environment. Two different psychologic attitudes were found in cases in which psychoanalytic treatment was given—one typical of melancholia, such as the pessimistic rejected attitude, and the other of the paranoid state, with feelings of being attacked or unjustly treated by others. A causal psychodynamic relationship between these emotional attitudes and the tendency to constipation had been assumed on the basis of the psychoanalytic material. In order to test the general validity of this causal connection, a group of 100 patients showing persecutory delusions and 100 patients suffering from schizophrenia without paranoia who were used as controls were investigated with reference to excremental habits and the attitude toward excremental function and food. It was shown conclusively that in the control group 26 per cent of the patients were constipated, as compared with 72 per cent of patients with persecutory delusions. These figures, taken in conjunction with the psychologic attitude toward the excremental functions and food expressed by these paranoid subjects, confirm the conclusion of the authors that the psychodynamic basis of constipation is the same in psychotic patients suffering from persecutory delusions as in those

with only traces of a paranoid attitude. The frequent constipation of patients suffering from persecutory delusions is conditioned mainly by conflict about anal sadistic tendencies, which they deny and project. The frequent deprecatory attitude and delusions about food are another manifestation of the projection of the anal sadistic impulses. A statistical study of 40 patients suffering from depression corroborated the clinical observations of the frequent coincidence of depression and constipation (76.5 per cent).

HART, New York.

PSYCHOGENIC ASPECTS OF SKIN DISEASES. JOSEPH V. KLAUDER, J. Nerv. & Ment. Dis. **85**:249 (Sept.) 1936.

One is more conscious of the skin than of any other organ, partly because it is the site of many sensations. Moreover, much concern is devoted to the beauty of the skin, and feelings of inferiority are found often in persons with even slight cutaneous lesions. On the other hand, decorations of the skin, such as tattooing and German student scars, are often acquired with pride. Conversely, the psyche has a great influence on the skin, since all varieties of cutaneous lesions have been reported after suggestion. Thus, frights are said to have produced ecchymosis, Raynaud's disease, urticaria and other lesions. Profound cutaneous anesthesia can be induced in some persons, such as the woman reported by Strümpell who could pick eggs out of boiling water without showing burns. Klauder and Brown have demonstrated that the reactivity of the skin is decreased in animals in a state of narcosis, and this is shown in man by the absence of itching and pruritus during sleep. Klauder does not agree, however, with the opinion of some authors that herpes zoster and psoriasis may have a psychogenic basis. Erythema and blushing, on the other hand, are often associated with psychic embarrassment, and Klauder believes that angioneurotic edema, urticaria and dermatitis or eczema are manifestations of unstable sympathetic nerve action. In the article several cases are briefly reported—one that of a woman who had itching of the body each Tuesday and Wednesday night. Her husband had died on a Wednesday night, having been moribund for twenty-four hours before. Klauder accepts the psychoanalytic interpretation that there is a sexual or lustful satisfaction in pruritus or that the condition may be a masochistic act. A considerable percentage of patients with pruritus vulvae or pruritus ani are psychoneurotic, such as the painter who experienced pruritus ani each time he made a public exhibition of his paintings. Menninger regarded many of the excoriations of neurotic patients as masochistically attenuated forms of suicide, in that the death instinct is thwarted of its purpose through the sacrifice of a part for the whole. He regards dermatitis factitia as a self-mutilative type of malingering, which serves as an externally directed aggression of deceit, robbery and false appeal, simultaneously. Alopecia areata and sudden whitening of the hair have been traced to severe fright.

Klauder concludes that it is incumbent on the dermatologist to envisage the patient as a living personality; attention should be given to circumstances associated with the onset of symptoms and with the environmental conditions in which the patient lives.

HART, New York.

THE PSYCHOLOGY OF JUVENILE PARETIC NEUROSYPHILIS. W. C. MENNINGER, Psychoanalyt. Rev. **23**:76 (Jan.) 1936.

In a previous study based on forty-three cases studied personally and six hundred and ten cases reported in the literature, Menninger recorded the observation that the mental picture most typical of juvenile dementia paralytica is progressive dementia. Delusions were present in 19 per cent of the patients, with 9.5 per cent expansive or grandiose and 4.3 per cent paranoid. Euphoria was present in 17.6 per cent of the patients, and depression, in only 8.6 per cent. Infantile personal

habits and mannerisms were frequent; conspicuous manual masturbation was commonly reported; 43.3 per cent of the patients showed untidy excretory habits; dancing, bouncing in bed, collecting waste and trinkets, stroking the hair, pulling at the nose or ears and grimacing were much more common in juvenile than in adult dementia paralytica.

These figures are significant in indicating differences in the mental picture in the juvenile form and that observed in the adult type. They suggest the special points to be studied in the psychologic picture of the juvenile form, namely, the dementing process, the *petites* expansive delusions, the rarity of depression and the frequency of infantile mannerisms.

The dementia of the juvenile form is due in part to organic destruction of the brain. In addition, there is evidence of the important mechanism of regression in the psychoanalytic sense, both of libido distribution (object-finding phases) and ego development. In psychosexual development the patient with juvenile dementia paralytica rarely reaches even the homo-erotic level, and in none of Menninger's cases did one reach adult heterosexual development. Often, an effort toward homosexual adjustment is to be observed, but in nearly every case it is apparent as the disease progresses that interest (libido) is withdrawn from the external environment and exhibitionism, sadism, masochism and auto-eroticism in other forms become more common. This regression is suggested by the early symptoms of the disease—dulling and withdrawal of former interest in persons and objects, sensitiveness and timidity. The regression is progressive to levels of simpler functioning, and as the disease reaches the terminal stage, there are nearly complete withdrawal of interest (libido) investment from the external environment and entire fixation on the patient (absolute narcissism). In contrast to the adult type of dementia paralytica, in which progressive deterioration usually results in elaborate compensatory efforts, such as delusions of omnipotence and other psychotic symptoms, the juvenile type reaches a primitive, infantile, auto-erotic, tube-fed, vegetative state, suggestive of an intra-uterine state.

The majority of patients with juvenile dementia paralytica show simple deterioration rather than the psychotic reaction usual in the adult form, for two reasons: 1. The ego ideal is incompletely developed and weakly differentiated at the age of onset of the illness in most cases of the juvenile type. 2. A stormy pathologic cerebral process may stir the psyche to a more aggressive compensatory activity than a slowly developing disease, which would result in deterioration rather than in mania or melancholia of the dementia paralytic type. This, indeed, must be the case in juvenile dementia paralytica.

Depression is infrequent and is rarely associated with self-depreciation and self-accusations, but there is loss of self-esteem, usually from thwarting or rebuff. Patients with juvenile dementia paralytica respond with a compensatory projection of their inadequacy. Likewise, the expansive delusions are poorly formed not because of immature development of the ego ideal alone. The child has not reached a point at which major conflicts may arise about potency or creativeness. The counterpart symptoms of euphoria and braggadocio are frequent, with a complacent attitude of well-being. It seems that this results through regression to a simpler level of life (ego development) at which prohibitions are fewer and the unconscious insight, previously perceived, may be ignored. Thus, it constitutes an overcoming of inadequacy and painful consciousness of the disease.

Probably the most important psychologic trauma experienced by patients with juvenile dementia paralytica is the recognition of mental failure, evidence of which constitutes one of the earliest symptoms. The patient talks of his mental failure without a real understanding of it. He reacts to the unconscious recognition of his loss first with depression and projection in mild ideas of reference, and occasionally in paranoid delusions; he then regresses to an earlier psychologic stage of development, at which the inadequacies can be glossed over and compensated for by euphoria and delusions of childish power and satisfaction.

KARPMAN, Washington, D. C.

THE SIGNIFICANCE OF THE RORSCHACH TEST. P. E. VERNON, Brit. J. M. Psychol. **15**:199, 1935.

The major thesis of this article is that the Rorschach method is not an empirical objective test, as claimed by German writers, but a psychodiagnostic instrument of the play technic type. Psychometrists have sought by this test to present a complete cross-section of the personality by testing in controlled situations a sufficient number of samples of objective behavior. This method of personality study does not fit into the genetic-dynamic approach of the clinician. It escapes from the more intellectualized verbal modes of expression and gives a nonverbal method that allows for a type of study of latent personality structures similar to that provided through analysis of dream material. In the treatment of children, nonverbal play methods have replaced the more verbal approaches and bear a close similarity to the Rorschach test. The study of children's drawings reveal many points of contact with Rorschach's analysis of ink blots.

The importance of the examiner, through the kind of rapport he establishes with his subject, makes him more than a mechanical recorder of responses. Individual variations not revealed in the final score become of great importance in revealing points of emotional conflict. Attempts at too rigid scoring and interpreting may omit some of these more intangible observations which are so important for the full interpretation of the method. Rorschach, for example, expected particular psychograms to be associated with particular types of mental deviation. However, empirical deductions apply only to gross distinctions and not to important subtle deviations, interpretation of which make the Rorschach method a more dynamic diagnostic instrument. This means that "the true value of the test is what each investigator can himself get out of it on the basis of his own intuitive ability and his experience in applying it and following up its significance in a large number of cases."

Vernon concludes that the Rorschach test is essentially a method of obtaining insight into the patient's mind rather than an empirical, psychometric instrument and that it is a great aid in diagnosis, particularly in the psychoneuroses.

ALLEN, Philadelphia.

THE IMPORTANCE OF DREAM-ANALYSIS FOR PSYCHOLOGICAL DEVELOPMENT. H. GODWIN BAYNES, Brit. J. M. Psychol. **16**:105, 1936.

Baynes discusses the teleologic view of psychic processes and contrasts it with the causal-reductive view supported by Freud. He regards them as "reciprocal, subjective viewspoints depending less upon the objective behavior of things than upon the psychological attitude of the investigator." He confesses to a "temperamental partiality" for the teleologic view as "richer in problems of interest" but is convinced that "every psychologist must employ both standpoints in order to render an adequate account of vital processes." He protests that the causal, mechanistic view is by no means necessarily as valid as many psychologists trained in the natural sciences regard it. Certainly today, when "even physics is having its doubts about 'physical causation' . . . it is time to wonder whether psychology must still be harnessed to an argument that has lost its exclusive validity even for the physical sciences." He describes an embryonic process, in which "living bodies . . . act purposively quite independently of mind," as an example of teleologic activity in the purely biologic field. He believes: "The whole problem of the action of mind upon body, or of body upon mind, will assume an entirely different complexion if we can rid our thought of the underlying assumption that body is identical with mechanism."

"Psychology," he says, "is the only science in which the function of cognition is identical with the object of cognition. . . . Because the psyche, which we are attempting to observe, is also our experience," the psychotherapist especially is forced "to employ borderline conceptions, which, although empirical and descriptive in character, embrace none the less the irrational factor of experience."

The unconscious is such a borderline concept, but to regard it as being all sufficing is not justifiable. The standpoint from which one approaches the concept must be defined, or one becomes lost in "luxuriant speculation."

Baynes regards the dream as "a product of autonomous psychic activity . . . proceeding from an unknown" rather than from an unconscious "part of the mind." Can this activity be teleologic? He subscribes to the principle of "co-ordinating totality" as the basis of individuality and regards the "objective character of the dream experience as directly subserving the integrating function of consciousness. . . . This faculty of the autonomous psyche to objectify subliminal processes or events in plastic symbolism [as in dreams] must be regarded . . . as an essential condition of analytical therapy." He insists that such objectified psychic material must be interpreted teleologically, or one "will exclude the psyche itself from our so-called psychology." To him, by definition psyche means soul, or "the inherent purpose of being." Hence, the dream is to be regarded as "primarily . . . an experience of individual psychology" in which the emotional tone, the degree of participation by the dreamer in the action and the type of energy conversion are important. He illustrates his point of view with an interpretation according to Jung of one of his own dreams.

Finally, he presents a brief discussion of the constructive or analogical method of Jung in which by "amplification" an immature "dream myth" is related to a parallel cultural pattern from general mythology. This method "invites the patient to emerge from his twilit neurotic sanctum, where he is closeted with his personal inadequacy, into the wide field of human history, where he is liable to find just that symbolic creation which, through its inherent correspondence with his own myth, will possess for him the redeeming value." The patient's subjective feeling of value is thus increased by giving widely accepted meanings to his symbolism.

Probably, he believes, "the retrogressive movement of the dream sequence back to . . . infancy can be viewed as a teleological quest for those functional elements of the original nature which have become dissociated and repressed and, therefore, need to be restored. . . . Under this viewpoint the dream remains constantly in allegiance to reality, and the work of salvage of deformed or neglected functions is undertaken with this end always in view."

Baynes concludes that ultimately one should learn that the causal-reductive and the teleologic approach to therapy are complementary instead of mutually exclusive.

ALLEN, Philadelphia.

A CASE OF RECURRENT ATTACKS OF PROLONGED SLEEP. M. S. JONES, J. Neurol. & Psychopath. **16**:130 (Oct.) 1935.

Jones reports the case of a woman aged 22, who suffered from attacks of prolonged sleep, lasting from one to six days. In addition, there were shorter attacks lasting about five minutes, cataplectic and fainting spells, vomiting, epistaxis and hysterical episodes of somnambulism and fugue. The recurrent attacks of prolonged sleep were constant. They were preceded and followed by malaise, sharp pain and a feeling of fulness in the head, nausea and vomiting, a feeling of constriction in the chest, salivation, sweating and epistaxis. The actual sleep state varied from drowsiness to deep sleep. The latter was accompanied by the loss of corneal reflexes, generalized anesthesia and the plantar extensor response, without incontinence or changes in the pupillary and deep tendon reflexes. Neurologic examination pointed to a functional rather than an organic type of illness, owing to such signs as shifting anesthesias, loss of pharyngeal, palatal and corneal reflexes and concentric narrowing of the fields of vision. Biochemical examinations revealed a low basal metabolic rate (— 20 per cent), a persistently low cholesterol content of the blood and a tendency toward acidosis. Psychologic investigations pointed to the psychogenic nature of the condition and the diagnosis of hysteria.

Jones agrees in the main with Kinnier Wilson in classifying cases of prolonged sleep with narcolepsy. The low cholesterol content is also characteristic of

narcolepsy. Symptoms of a vagal nature, presented in this case, may be explained by Hess' theory of the reflex character of sleep, experimentally induced by stimulating the parasympathetic fibers. However, Jones concludes by emphasizing the psychologic element. He regards the sleep state as another manifestation of dissociation, functioning as an escape from reality.

N. MALAMUD, Ann Arbor, Mich.

ORGANIC ALTERATIONS IN SCHIZOPHRENIA. EMILIO PELAZ MARTÍNEZ, Arch. de neurobiol. **15**:457, 1935.

The author studied 145 patients, dividing them into three groups: those in whom the schizophrenic process was active (117), those in whom it was inactive (18) and those in whom it was reactive (10). He found that no somatic alteration is specific for schizophrenia. The permeability of the meninges seems to be the most useful observation in diagnosis.

The spinal fluid showed abnormality in 69 per cent of cases of active and in 40 per cent of cases of inactive schizophrenia. The meningeal permeability in the active forms had a high quotient in 81 per cent of cases. The average quotient for the active and for the inactive form was 3.4, while the reactive forms had an average of 3.1. Hypocalcemia was encountered in catatonia, while other forms of schizophrenia showed a normal calcium level. Lysemia in the active forms passed the upper normal limits in 47 per cent of cases, while the inactive forms had hypolysemia. The cholesterol content was raised in 45 per cent of cases of the active form, but in grave crises there was hypocholesteremia. In the sugar content of the blood there were oscillations during fastings, with crises of spontaneous hyperglycemia and hypoglycemia. The most frequent alteration in the dextrose tolerance curves was prolongation of the curve, which was delayed in recovering its original value. With epinephrine the author frequently noted attentuated curves, With insulin the most frequent finding was the retarded curve. Analysis of the gastric secretion showed frequency of hypochlorhydria and absence of free hydrochloric acid in catatonic stupor, with negativism to eating. In active schizophrenia there was a tendency to a low level of hydrochloric acid, and in the inactive form, a tendency to hyperchlorhydria. Blood studies showed a slight leukocytosis in 41 per cent of cases of the active form. In 40 per cent there was lymphocytosis with neutropenia. Study of the inactive form gave analogous results. There was a slight tendency to erythrocytosis in active forms, but with low levels of hemoglobin. The sedimentation rate was increased at the beginning of schizophrenia in the majority of cases, with accompanying loss of weight. As organic and psychic improvement takes place, there are a return to normal of the sedimentation rate and a gain in weight.

ALPERS, Philadelphia.

SOCIAL PROGNOSIS OF SCHIZOPHRENIA ON THE BASIS OF ENCEPHALOGRAPHIC FINDINGS. RUDOLF LEMKE, Arch. f. Psychiat. **104**:89 (Sept.) 1935.

In a number of patients with schizophrenia the disease process manifests itself in the form of an acute attack, at the expiration of which the patient recovers to the extent that he can return home and take up his work, showing little or no defects. Lemke attempts to find criteria which will help in differentiating cases of this type from those of chronic, deteriorating psychoses. He studied two sets of patients: 1. One hundred and twenty-six patients who had been admitted to the hospital and discharged during the fifteen years preceding the study. He found these were divided into four groups: Thirty-four per cent were at home and adjusting well; 19 per cent were at home but were mentally sick; 27 per cent were in hospitals, and 20 per cent had died. 2. One hundred and thirty-two patients admitted to the hospital during the two years preceding the study and then discharged from the hospital. In all these cases Lemke concentrated on five sets of factors, which he tested for their validity as criteria: (1) physical make-up, (2) hereditary predisposition, (3) prepsychotic personality, (4) exogenous (psychic) factors and (5) encephalography. In relation to the

physical make-up, he found that the theory advanced by Kretschmer that schizophrenia has a predilection for asthenic persons and athletes does not hold true, since in his case there were 25 per cent of the asthenic, 20 per cent of the pyknotic, 25 per cent of the athletic and 2.6 per cent of the dysplastic type and 26.9 per cent mixed forms. Furthermore, the statement made by some authors that in persons of pyknotic body build who suffer from schizophrenia the illness shows an acute course tending toward improvement is not proved to be correct by Lemke's material. The body build, therefore, does not seem to have any validity as a criterion for prognosis in the disease.

Hereditary factors are of much greater importance. A family history of mental disease was much more frequent in the cases in which the prognosis was poor. Furthermore, a history of schizophrenia in the family was particularly frequent in cases in which the prognosis was poor and much less frequent in cases in which there was recovery.

In the study of the pre-psychotic personality, Lemke stresses particularly such factors as irritability, excitability, withdrawal from society, unscrupulousness, cold affect and paranoid features. Here, too, it was found that these features were much more common in cases in which there was a poor prognosis than in those in which recovery and readjustment resulted. Of particular importance is the fact that when both these features are present, that is, a premorbid personality showing the features mentioned and heredity tainted with mental disease, especially schizophrenia, the probabilities are that the process, regardless of whether the onset is acute or chronic, will lead to continuous and progressive deterioration.

Encephalograms were made in 100 cases. These were divided into five groups. In the first three groups, composed of 50 cases, were variations of what might be considered the normal picture. The other 50 cases were divided into two groups; in 29 there was a moderate degree and in 21 a high degree of internal hydrocephalus. The prognosis in these cases is closely related to the encephalographic findings, in such a way that all cases in which a good prognosis was shown were limited to the first three groups, whereas in the last two groups most cases were those of a chronic, deteriorating type.

Added to the hereditary and prepsychotic personality factors, the encephalograms make the distinction in terms of prognosis much more certain.

MALAMUD, Iowa City.

PSYCHOPATHOLOGIC FEATURES OF THE AMNESIC SYNDROME (CONFABULATIONS OF PATIENTS WITH KORSAKOFF'S PSYCHOSIS). G. KÖRNER, Monatschr. f. Psychiat. u. Neurol. **90**:177 (Jan.) 1935.

Körner proceeds from the views of Bürger-Prinz and Kaila that Korsakoff's syndrome is based on a unitary structural disturbance which extends into all psychic fields. This disturbance is characterized by rapid tiring of the need for finding the meaning of things and by a lack of personality, with passivity and paralysis of vital activities. In addition, there are changes in the temporal progression of mental processes, diminution of the quantity of activity, loss of differentiation and difficulty in *Gestalt* formation. Körner shows that the confabulations fit into this general psychiatric picture. They owe their origin to increased suggestibility, preservation of the ability to react to outside stimulation and readiness to respond in an uncritical manner. The factors which are responsible for the increased suggestibility are: (1) an impersonal and aimless manner of living that is lacking in spontaneity; (2) inability to bring different complexes of experience potentially present into relation with one another, and (3) lack of appreciation of the significance of given situations and inability to change them actively or to react spontaneously to them in an adequate manner. The retention of the ability to react to outside stimuli forms an integral part of the clinical picture of Korsakoff's psychosis. The content of the confabulations is always related to actual experiences. The patient sees himself in a past situation and projects the real environment uncritically into the past situation, or he reacts to an indifferent

question by recalling experiences that occurred most frequently in the past. As insight is gained, the confabulations become progressively less prominent. This is not surprising, for increasing insight is an indicator of a partially preserved personality, which serves as a point of orientation for all assertions.

ROTHSCHILD, Foxborough, Mass.

THE SCHIZOID PERSONALITY. JOSEF BERZE, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:600 (Sept.) 1935.

The schizoid state does not differ merely quantitatively from schizophrenia. There is a fundamental biologic difference. The primary insufficiency of psychic activity or hypotonia of consciousness of the schizophrenic patient is not seen in the schizoid person. Neither does one encounter the disturbance in thinking which have been emphasized by Bleuler. The central disorder in the schizoid person is a defective fusion of experiences and appropriate affect. This disturbance has also been described as a failure of intrapsychic synergy between the affective and the cognitive aspects of behavior. It is an anomaly of psychic development based perhaps on a poor anlage. For some reason, there is inordinate binding of affect to instinctual strivings. The precocious shutting-in of these persons is noted.

Berze denies that schizoid persons show serious defects in thinking, though they devote themselves readily with great affect to particular lines of thought. They are often unusually stubborn and hard to convince. There is always the danger of losing contact with reality, as they seek to defend their own position. They attend to and grapple with real problems not within their spheres of interest, though not with the gusto and feeling accompanying the activities in which they are interested. They seem always intolerant of discussions and conversations of little interest to them. They often lead others into considering their pet subjects. They have a desire for power and frequently show grandiose tendencies. They feel keenly the onus of undesired responsibilities and crave for freedom. They abhor doing things they dislike, fret under parental authority and actively and vehemently oppose whatever runs counter to their wishes. They enjoy practical jokes at the expense of others and, in sadistic fashion, delight in the resulting pain, anguish and distress of the victims of such horse-play.

Puerilism is a noteworthy characteristic of the schizoid person. He cannot play like the mature adult. The harmless diversions of the grown-up do not appeal to him. Music, art and literature hold no attraction. The spontaneity of the play activity is often marred by an undercurrent of anger, and even of malice. It is due to an almost constant desire to excel. These persons lack a sense of humor.

As a result of the fundamentally disordered noothymic synergy, the moral behavior of these persons becomes defective. They find it impossible to mobilize their intellectual acquisitions and fuse them properly with their affective experiences. A remarkable defect of the personality results. The affective responses are occasionally infantile and give the impression of the existence of a so-called second nature. This almost double personality alternates automatically in reaction to actual stimuli. Such posing and the existence of different facets of the same person are not an unknown variant of normal behavior, though perhaps it is more striking in the schizoid person.

Berze describes a typical psychotic reaction pattern which he has often noted in schizoid persons. These episodes are usually of short duration and resemble more closely the affective psychosis than the schizophrenic picture. Anxiety alone is rare. The dominant feature in the clinical picture is an unusual combination of anxiety, anger and irritability. In one case it could be described best as a state of bewilderment. The mental content is usually simple. Flight of ideas and other disorders in the stream of thought encountered in true cyclothymic persons are not present. Psychomotor agitation is always present. Close scrutiny of the clinical complex reveals irritability as the dominant affective state. Berze is not inclined to accept the existence in these cases of a combination of schizoid and

cyclothymic tendencies. At times paranoid ideas appear. The sensitivity and querulousness of the schizoid person occasionally result in behavior similar to that of the paranoid psychopath. The schizoid make-up is a constitutional defect. Schizophrenia is a definite disease process. SAVITSKY, New York.

Meninges and Blood Vessels

SIGNIFICANCE OF SEROLOGIC TYPES AMONG MENINGOCOCCI. SARA E. BARNHAM, J. A. M. A. **108**:92 (Feb. 27) 1937.

According to Barnham, classifications of meningococci worked out in the years 1909 to 1918 represent true serologic relationships which can be plainly recognized today. Certain changes in these relationships have taken place: Type I and type III have become so closely interrelated that separation into two types no longer seems to be of value in practical, every day work. This I-III, or A, group has become markedly predominant in nearly all parts of the world. On the other hand, types II and IV have, in the United States at least, become distinct from each other, so that they represent two separate groups. There seem to be three types of meningococci: I-III, II and IV. The designation of group B cannot be well applied to a combination of two such distinct groups as types II and IV. Studies seem to indicate a greater number of carriers of type II strains. This large number of carriers of strain II in proportion to the very small number of cases of type II infection raises this question: Is type II less pathogenic than the I-III group? This idea finds some support in the following fact: Although 70 per cent of all strains isolated from blood were those of type II, in nearly all cases of meningococcic endocarditis in which the type has been determined the organism belonged to the I-III group. There is some evidence that type II is especially likely to be responsible for septicemic and generalized forms of meningococcic infection, which may be relatively mild or chronic. Both the endotoxins of Gordon and the soluble toxins reported by Ferry are produced to a greater extent by the I-III group. Thus, one finds at present predominance of that group of meningococci which seems to be both more invasive and more toxic.

EDITOR'S ABSTRACT. [J. A. M. A.]

SIGNIFICANCE OF DIMINUTION OF SPINAL FLUID SUGAR IN TUBERCULOUS MENINGITIS. M. WEICHSEL and GERTRUD HERZGER, J. Pediat. **9**:763 (Dec.) 1936.

Weichsel and Herzger observed the diagnostic value of the sugar content of the spinal fluid in cases of tuberculous meningitis. The method used for the determination was that of Jensen and Hagedorn. Progressive diminution of the sugar content of the fluid was found from the time of first observation to the fatal termination of the illness. In this decline there was in many cases a slight increase about two weeks before death, and then a final drop. The authors believe that the diminution of the sugar of the spinal fluid is an early diagnostic sign, since in several cases the value for the sugar showed a decline from twenty-five to thirty days before the death of the patient. In most cases the decrease in the sugar content followed a rise in the amount of globulin and an increased cell count. After intraspinal injection of a 5 per cent solution of dextrose in children with tuberculous meningitis, a response in blood sugar was observed, which can be compared with that found after intramuscular injection or after absorption of sugar from the intestinal tract. The sugar content of the cerebrospinal fluid at the end of a spinal puncture gave almost the same value as at the beginning, and repetition of the puncture after one hour usually gave no higher amounts. After an artificial increase of the sugar in the blood, the ratio between the sugar in the blood and that in the spinal fluid remained the same. The absolute augmentation of the dextrose in the cerebrospinal fluid was low. The experiments tend to show that the chief cause of the diminution of sugar is not increased glycolysis but disturbance of the barrier between the blood and the spinal fluid. EDITOR'S ABSTRACT. [J. A. M. A.]

RÔLE OF SCURVY IN ETIOLOGY OF CHRONIC SUBDURAL HEMATOMA. T. H. INGALLS, New England J. Med. **215**:1279 (Dec. 31) 1936.

In studying the incidence of chronic subdural hemorrhage as reported by various authors, Ingalls finds that it occurs primarily in infants, chronic drinkers and psychotic persons. Subclinical scurvy may exist before clinical manifestations and roentgenographic changes of chronic subdural hemorrhage become apparent. One of the group of nine infants studied at the Children's Hospital in Boston is excluded, as there was a history of hemorrhage at birth. Five of the eight remaining patients were cared for in institutions or by foster mothers; it was specifically recorded that six infants had rachitic rosaries of varying degrees. Roentgenograms of the long bones were available for study in five of the infants, and roentgenographic evidence of scurvy was elicited in three. Active scurvy could not be demonstrated readily, since the essence of the concept is that of a chronic, low grade process. One might say that chronic subdural hemorrhage as encountered clinically and at necropsy is an end-stage, far removed from the initial series of events. The scorbutic process itself may have been arrested, without obviating the effects of repeated cerebral hemorrhage. It is not unreasonable to assume that close scrutiny of the diet of alcoholic addicts and of psychotic patients would often reveal deficiency of vitamin C—an observation much more subject to objective proof in early life. Studies of cevitamic acid levels in the blood and urine for the determination of the degree of saturation with the vitamin offer new methods of investigating latent scurvy. The following sequence of events seems to be concerned with the production of idiopathic chronic subdural hematoma: Underlying bleeding diathesis is postulated in most cases on the basis of scurvy. Free subdural bleeding is produced by a definite or insignificant trauma to the head causing either disruption of arachnoid invaginations into the dural sinuses or rupture of a bridging vein. Organization and removal of the clot are impeded by the scorbutic process, resulting in a neomembrane surrounding free blood. Repeated trauma and remission and exacerbation of the scurvy modify the disease. Late symptomatology is occasioned by enlargement of the semipermeable sac, following the slow breakdown of red cells and reduction of free hemoglobin into smaller molecular aggregates with the passage of time.

EDITOR'S ABSTRACT. [J. A. M. A.]

CHRONIC MENINGITIS IN WEIL'S DISEASE. FREDERICK MURGATROYD, Brit. M. J. **1**:7 (Jan. 2) 1937.

The diagnosis of Weil's disease was made in the case of a farmer aged 35 who had jaundice and persistent fever and in whose urine Leptospira icterohaemorrhagiae was observed. Four months later, after several remissions and exacerbations, there developed low grade meningitis. Leptospira could not be demonstrated in the spinal fluid by direct examination, but the organism was recovered from the blood of guinea-pigs which had been inoculated with the spinal fluid. The disease also developed in guinea-pigs inoculated with the patient's urine. After the intrathecal and intramuscular administration of antileptospiral horse serum, the patient recovered.

ECHOLS, Ann Arbor, Mich.

THE VIRUS AETIOLOGY OF ONE FORM OF LYMPHOCYTIC MENINGITIS. G. M. FINDLAY, N. S. ALCOCK and RUBY O. STERN, Lancet **1**:650 (March 21) 1936.

Findlay, Alcock and Stern isolated a virus from the cerebrospinal fluid of two patients suffering from obscure nervous symptoms associated with an increase of lymphocytes in the cerebrospinal fluid. Intracerebral inoculation of monkeys, mice, rats and guinea-pigs with the virus caused fatal infection. Postmortem examination revealed intense round cell infiltration of the meninges, choroid plexus and ventricles. When mice were inoculated intraperitoneally, the virus caused no symptoms but remained for several weeks in the spleen and kidneys. It was excreted in the urine of mice and passed through the lightly scarified skin. The

human and mouse strains isolated by the authors behaved in the animal in the same way as the American virus described by Armstrong. Serums obtained in cases occurring in man in England contained bodies immune to the American virus and to the English mouse strain virus. WATTS, Washington, D. C.

RÔLE OF THE BOVINE TYPE OF BACILLUS IN THE ETIOLOGY OF TUBERCULOUS MENINGITIS IN CHILDREN. E. LESNÉ, A. SAENZ, M. SALEMBIEZ and L. COSTIL, Arch. de méd. d. enf. **39**:798 (Dec.) 1936.

Lesné and his associates found that in the majority of cases of tuberculous meningitis there are persons in the immediate surroundings of the child who are giving off bacilli. Often there is no direct evidence of contagion. The bovine type of bacillus is possessed of a virulence equal to that of the human. This is especially true of Scandinavian countries and of England, where the consumption of crude dairy products is large. In 9 of 130 cases studied the bovine type was furnished, cultures of which grew slowly and showed far less abundant colonies than the human type. An intravenous injection of this type into a calf produced visceral and especially serous tuberculosis within four months. The liver and spleen were studded with numerous tuberculous nodules. The serosa and the renal parenchyma likewise presented disseminated nodular lesions. The mesenteric ganglia were hypertrophic, and the visceral membrane showed copious new formations. Similar formations occurred in both pleurae and in the bronchial and mediastinal lymph nodes. No atypical forms were observed, and it could be said that the source of contamination must be contaminated milk. Up to 100,000 virulent bacilli were counted for each cubic centimeter of milk. The manner of treating the udders and keeping the animal clean is mostly responsible, and it has been found that not only the milk but other dairy products, such as butter and cream, carry the contamination. The observation was also made that all the children had stayed in the country and for many months had lived mostly on dairy products. In all these cases the cerebrospinal fluid contained the bacilli, and it was demonstrated that the incubation of the liquid on elective mediums gave results in 100 per cent of cases. More attention should be paid to the treatment of milk at the place of production. EDITOR'S ABSTRACT. [J. A. M. A.]

ACUTE IDIOPATHIC, OR EPIDEMIC, SEROUS MENINGITIS. O. STENDER, Deutsche Ztschr. f. Nervenh. **141**:217, 1936.

Serous meningitis has not been fully recognized as a disease entity. A disease of similar description, however, has occurred in small, epidemic-like outbursts in various European countries. Stender studied fifteen cases occurring in the first six months of 1936. These were characterized by: an acute febrile onset, with meningitic signs, which was independent of other infectious diseases, such as influenza; lymphocytosis with a count of from 40 to 1,000 lymphocytes per cubic millimeter of spinal fluid, and a slight increase in the amount of globulin in the spinal fluid. The spinal fluid pressure was sometimes elevated to 600 mm. Cultures of the spinal fluid and vaccination of animals gave negative results. The course of the disease was usually benign, though transient involvement of the cranial nerves and pyramidal tracts and convulsions occurred. Drainage of the spinal fluid gave immediate relief and seemed the only therapy necessary. There are no reports of pathologic changes. Stender believes that the cases he studied represent an infectious disease of unknown origin. HOEFER, Boston.

TUBERCULOUS ENCEPHALITIS OF THE STRIATUM ASSOCIATED WITH A PARKINSONIAN SYNDROME. I. SCHEINKER, Deutsche Ztschr. f. Nervenh. **141**:227, 1936.

Scheinker reports a case of subacute encephalitis of about four months' duration. The neurologic features were those of a parkinsonian syndrome, with occasional choreiform features and terminal coma. The clinical course showed intermittent

fever, with occasional remissions, but the temperature was constantly high before the end. Autopsy of the brain showed bilaterally symmetrical primary tubercles in the striopallidum. Histologic examination of these foci showed caseous central masses surrounded by spindle cells, forming a fibrous tissue network, and occasional Langhans giant cells. In the periphery lymphoid cells and single plasmocytes were seen. The surrounding brain substance showed numerous perivascular lymphocytic infiltrations. Another isolated focus in the lateral region of the pons showed more chronic changes, with extensive formation of granulation tissue resembling closely a focus of miliary tuberculosis. Small miliary foci were observed around the lesions in the basal ganglia. Stains for glia showed an increase in the glia cells with degeneration, colliquative necrosis and edema. A few small hemorrhages were present. The substantia nigra was normal. No other foci of tuberculosis were obesrved in the body. It is pointed out that primary tuberculous involvement of the brain is rare.

HOEFER, Boston.

MENINGEAL REACTION IN ERYTHEMA NODOSUM. D. VON MÓRITZ, Monatschr. f. Kinderh. **67**:255 (Nov. 28) 1936.

According to von Móritz, the etiology of erythema nodosum is not entirely established; for, whereas some assume a special, as yet unknown agent, others think that it is of tuberculous origin and represents a form of subcutaneous tuberculid and still others consider it an allergic or a parallergic cutaneous reaction, usually on the basis of tuberculous allergy. The author thinks that, regardless of whether the one or the other opinion is accepted, it is certain that erythema nodosum is not a local cutaneous disorder but a partial manifestation of a general reaction of the organism. The general symptoms, such as fever, headaches, loss of appetite and severe depression, which accompany the erythema nodules, corroborate this. The reaction capacity of the skin and of the entire organism is changed. The sedimentation rate of the blood is accelerated; there are leukocytosis and a slight deviation to the left. Roentgenoscopy reveals perihilar infiltration in some cases. The observation of meningeal symptoms in a case of localized erythema nodosum induced the author to give especial attention to these symptoms and to resort to chemical examination of the spinal fluid. He studied the spinal fluid in ten cases. A tabular report of the results indicates that the pressure of the fluid was increased, probably due to an increase in the quantity of the fluid. The author thinks that in the cases examined the meningitic reaction as well as the erythema nodules and the perihilar infiltrations were all manifestations of an allergic reaction. Intracutaneous tests with increasing doses of tuberculin in three of five tuberculous children resulted in meningeal symptoms, which disappeared after a few days or a week. In these cases, examination of the cerebrospinal fluid revealed increased pressure but no other pathologic changes. Von Móritz thinks that the meningeal symptoms were of tuberculotoxic or allergic origin, in that the allergy of the organism was suddenly increased in response to the intracutaneous injection of tuberculin. He evaluates the significance of these observations in connection with tuberculosis meningitis and points out that the anamnesis frequently reveals erythema nodosum in cases of tuberculous meningitis.

EDITOR'S ABSTRACT. [J. A. M. A.]

Diseases of the Brain

ACUTE EPIDEMIC ENCEPHALITIS: A CLINICAL STUDY OF 160 CASES. H. A. SLESINGER, Am. J. M. Sc. **192**:225 (Aug.) 1936.

An epidemic of acute encephalitis which occurred in the Windber, Pa., district during the summer of 1935 is described. The disease is undoubtedly a virus infection transmitted by human contagion, by means of droplet infection. The period of incubation varied from three to ten days; in most cases it was about four days. The infection occurred more often in males (ninety-eight males and sixty-two

females). Only seventeen cases occurred after the age of 30. Headache, usually occipital, and nausea or vomiting were the outstanding symptoms. Photophobia, pain in the eyeballs, pain in the posterior cervical region, backache, abdominal cramps, muscular pains, nervousness, sleeplessness and vertigo were frequent complaints. Convulsions or coma occurred in only one case. There was a notable absence of positive physical signs. One constant positive finding was the typical injection of the soft palate. The temperature varied from normal to 102.4 F. There was usually leukopenia. The spinal fluid pressure varied; globulin was present in varying amounts in all cases. In twenty-two cases there were over 20 cells per cubic millimeter, all of which were lymphocytes. Three clinical types were differentiated: (1) the mild, or abortive, type; (2) the moderately severe, or usual, type, and (3) the severe, or fulminating, type. Autopsy in one case showed acute hemorrhagic meningo-encephalitis. The prognosis is usually good. The significant aspect of the treatment was that patients who received intramuscular convalescent serum recovered more quickly than those who did not.

MICHAELS, Boston.

INCIDENCE AND DIFFERENTIAL DIAGNOSIS OF HYPOGLYCEMIC CONVULSIONS. EUGENE ZISKIND, BENJAMIN S. HOLLOMBE and RUTH O. BOLTON, Am. J. M. Sc. **192**:600 (Nov.) 1936.

Of 200 cases of epilepsy, the etiology was unknown in 113 and known in eighty-seven. Only thirty-one patients (15.5 per cent) presented blood sugar readings below 70 mg., and four (2 per cent) below 60 mg. In no instance did there develop clinical symptoms of hypoglycemia after a thirty-six hour fast. Injection of insulin in sufficient doses in forty cases failed to result in reproduction of seizures. In the differential diagnosis of hypoglycemic convulsions and other types, the following criteria are important: (1) prodromal symptoms of the mild hypoglycemic type, such as hunger, a sense of ill-being, weakness, palpitation, tremor, perspiration, confusion, restlessness and various focal neurologic symptoms; (2) qualitative and quantitative variability in the nature of the attacks, and (3) relationship of the attacks to feeding. The longer the interval since the preceding meal, the greater the likelihood of hypoglycemic symptoms. The dextrose tolerance test is not of much aid, as was demonstrated in a series of cases in which four hour dextrose tolerance tests were performed.

MICHAELS, Boston.

INTRACRANIAL PRESSURE IN HEAD INJURIES. ARTHUR A. ZIEROLD, Arch. Surg. **31**:823 (Nov.) 1935.

On the basis of readings of pressure obtained by lumbar puncture in a series of 128 cases of injury to the head, the following conclusions are reached: In cases of severe injury to the head the abnormal intracranial pressure is not frequent, and only in a small percentage of cases will it exceed 300 mm. of mercury. Abnormal intracranial pressure is not frequent in cases of fatal termination, nor is it a frequent cause of death. Unconsciousness is not in itself evidence of abnormal intracranial pressure, nor is the period of unconsciousness a measure of the degree of intracranial pressure. Unless abnormal intracranial pressure develops rapidly and is of sufficient degree to approximate the blood pressure, changes in pulse rate and blood pressure do not develop, and such changes cannot be considered as satisfactory evidence of abnormal intracranial pressure. Neurologic findings, such as changes in pupillary reflexes and changes in reflexes elsewhere, are not signs of increasing intracranial pressure. Increased intracranial pressure is almost invariably attended by blood in the spinal fluid. When abnormal intracranial pressure occurs, it is the result of hemorrhage—extradural, subdural or within the substance of the brain. It is not probable that abnormal intracranial pressure of a degree sufficient to endanger life is susceptible to treatment by spinal drainage or by the use of hypertonic solutions. It also appears reasonable that such few abnormal intracranial pressures as occur which are of sufficient degree to endanger life are best treated surgically.

GRANT, Philadelphia.

DERMOID AND EPIDERMOID TUMORS (CHOLESTEATOMAS) OF THE CENTRAL NERVOUS SYSTEM. J. GRAFTON LOVE and JAMES W. KERNOHAN, J. A. M. A. **107**:1876 (Dec. 5) 1936.

Love and Kernohan base their discussion on a clinical, surgical and pathologic study of fifteen cases of congenital epithelial tumor (epidermoid, dermoid, pearly tumor and cholesteatoma) of the central nervous system that had been verified microscopically at the Mayo Clinic. Fourteen of the fifteen patients who harbored these tumors were operated on by the members of the neurosurgical staff of the clinic, with three postoperative deaths. Fourteen of the tumors were intracranial. One dermoid occurred in the spinal cord. The average age of the patients who had a dermoid was 22.3 years at the onset of symptoms, and the average age of patients who had an epidermoid was 20 years at the time of onset. The average duration of symptoms was sixteen years in cases in which an epidermoid was present and eight and a half years in cases in which a dermoid was present. Twelve of the fourteen patients who had a congenital epithelial tumor (dermoid or epidermoid) in the head complained of headache. Only two patients had had convulsions; both of these patients had a tumor that was situated in the basofrontal region. Twelve patients displayed definite alterations in their mental reactions. A congenital intracranial dermoid or epidermoid should be suspected in any case in which mental disturbance is associated with headache that has been present for a long time and suggests increased intracranial pressure. Five of the patients had edema of the optic disks at the time they were examined at the clinic. One had an associated defect in the field of vision which was sufficiently characteristic to localize the tumor. There are no criteria for making a correct diagnosis of the type of intradural tumor prior to operation. The relationship of trauma to this tumor is not clear. Trauma to the region of such a tumor doubtless will influence its growth, but injury in itself is not believed to be sufficient to cause the tumor.

EDITOR'S ABSTRACT.

MENTAL SYNDROME OF CORPUS CALLOSUM TUMORS. BERNARD J. ALPERS, J. Nerv. & Ment. Dis. **84**:621 (Dec.) 1936.

Most observers agree that it is well nigh impossible to indicate a group of symptoms or signs which are characteristic of involvement of the corpus callosum. The most suggestive symptoms lie chiefly in the mental sphere. However, many of those which are attributed to the corpus callosum are characteristic of disease of the frontal lobe. Alpers and Grant have drawn attention to the inability of patients with tumors of the corpus callosum to concentrate, to focus and maintain attention for any length of time and to correlate more or less complex ideas. Alpers describes two cases of patients dying of tumor of the corpus callosum, in one of which the growth was confined to the anterior part of the callosum. The following mental symptoms were prominent: inability to concentrate, difficulty in thinking and imperviousness to stimuli of all sorts. The seeming indifference to all happenings in the external world was not due to aphasia, for understanding of speech was still retained. The response to questions was irrelevant, and the patient's attitude was frequently silly. The accompanying changes in personality probably resulted from invasion of the frontal lobe and increased intracranial pressure.

HART, New York.

PROGRESS IN NEUROLOGY IN 1934. J. LOMAN, New England J. Med. **213**:1238 (Dec. 19) 1935.

The most important advances in neurology during 1934 were: the work of Brodie and Elvidge on anterior poliomyelitis, demonstrating the portal of entry and the neurogenic distribution of the virus; Petersen's studies on the climatic factor in interpreting the symptoms of migraine, multiple sclerosis and tabes; physiologic studies on epilepsy and migraine, with therapeutic appraisal of the muscular dystrophies, and the results of investigation of the 1933 St. Louis epidemic of encephalitis B.

Brodie and Elvidge proved that the portal of entry and spread of the virus in anterior poliomyelitis was by way of the olfactory nerve and not by the spinal fluid. Paralysis was common in the groups from 6 to 25 years of age, and 71 per cent of the cases were in the group from 4 to 15 years old. Petersen regarded multiple sclerosis as meteorologically induced and due to vasomotor spasm in unstable persons. He stated further that attacks of migraine are more common with polar infalls and changes in barometric pressure. Weinberg reported good results in 12 patients with multiple sclerosis from the intraspinal use of lecithin. Neymann and Osborne recorded improvement in patients with this disease who were treated with diathermy, roentgentherapy and electrotherapy. Gibbs, Lennox and Gibbs showed that cerebral vascular spasm is not an important precipitating factor in epilepsy. Engel, McQuarrie and Ziegler pointed out that epileptic attacks are dependent on water and mineral metabolism. Jacobsen obtained seizures in 40 cases when he succeeded in raising the body weight by from 3 to 6 per cent by ingestion of water. Petersen associated migraine with sudden alkalosis and vascular spasm, together with leakage of potassium salts from the blood. Paskind disclosed no special relation between migraine and epilepsy.

Lennox, in a study of 39 cases of migraine in men and 6 in women, noted relief in 40 in from fifteen to thirty minutes after intravenous administration of gynergen. The action of the drug is due to paralysis of the motor sympathetic fibers, thus relieving the spasm.

Muckenfuss, Armstrong and Webster isolated a number of strains of a virus that seems to be the etiologic agent in the 1933 St. Louis epidemic of encephalitis B. Leake, Musson and Chope expressed the belief that individual susceptibility is more important than contagion in this disease. Intense capillary congestion, according to McCordock, Collier and Gray, is the outstanding pathologic change. Neal suggested the use of formaldehydized herpes virus in treating this disease and warned against the use of malaria and bulbocapnine. Sauter discussed the fate of 40 patients who survived an acute attack of this disease.

Posttraumatic symptoms may be evaluated and in some cases relieved by encephalography. Dyke and Davidoff described an improved encephalographic technic. A roentgen plate is taken after 20 cc. of air has been injected. This is an index of the total air volume necessary. Leary pointed out that subdural hemorrhage is relatively common and that alcohol was a factor in 27 of 50 cases. Munro reviewed 62 cases and implicated trauma as the chief cause, the diagnosis usually being made at operation. Only one half of the patients had an elevated spinal fluid pressure, and about one half had subarachnoid bleeding. The mortality was 100 per cent for 22 patients in whom there was no surgical intervention; only 41 per cent of 39 patients died after operation. In 120 of 200 patients Russell found that concussion symptoms were common. Epilepsy occurred in 3.5 per cent of these cases.

Grinker and Kandel, on the basis of 50 cases of pernicious anemia in which treatment was given for several months, concluded that liver is not efficacious in preventing degeneration in the central nervous system. O'Leary noted that in 90 per cent of cases neurosyphilis can be controlled by arsphenamine, bismuth and mercury. Normal results from examination of the spinal fluid after two years suggest that clinical neurosyphilis will not develop. Spiegel recommended the use of acetarsone in the treatment of neurosyphilis. Yates, from an analysis of 56 cases, expressed the belief that arsphenamine, bismuth and mercury are preferable to malaria. Claude and Masquin reported that of 327 men with dementia paralytica 62 per cent showed improvement with malaria treatment after a period of observation of eight years. Kuhns reported experience with treatment with the electric blanket of 230 patients with dementia praecox during four years. He regarded 72 per cent as showing definite improvement.

Dandy recommended section of the posterior half of the sensory root of the gasserian ganglion in trigeminal neuralgia. He stated that sensation of the face is not affected. Only 8 of 300 patients had recurrences. Dyes reported good results in 17 of 20 patients treated with high voltage roentgen radiation. The

patients were relieved for from three and a half to eleven years. Caldwell recommended trichloroethylene in this condition.

In regard to muscular dystrophy and myasthenia gravis, Nevin stated that the creatine-creatinine metabolism factor of Remen is secondary. Phosphorus plays an important rôle in both conditions. Kostakow obtained good results in 17 cases of myasthenia gravis from the use of amino-acetic acid.

Lightning and electricity, according to Critchley, may affect the central nervous system by causing focal petechial hemorrhages, chromatolysis of pyramidal cells, dilatation of the perivascular spaces, fragmentation of peripheral axons and softening of the brain tissue. Diffuse involvement is called "electrotraumatic encephalomyelitis." Peripheral nerve lesions and various psychoses may occur.

KRINSKY, Boston.

THE HAEMATOLOGY OF CONVULSIONS. ARTHUR GUIRDHAM and A. W. PETTIT, J. Ment. Sc. **82**:371 (July) 1936.

Blood counts were made on eight patients with epilepsy and on two normal persons used as controls, during a period of from twenty to fifty days. While in the normal subjects used as controls the leukocyte count varied from 4,000 to 8,000, in the epileptic patients it varied from 4,000 to 20,000, with an average variation of 9,017. Even if one allows for the fact that the normal variation may be as high as 100 per cent, the range of variations observed in epileptic patients was higher and pointed to definite leukocytosis. The leukocytosis corresponded with the occurrence of fits. The increase in the white cells was due largely to the increase in lymphocytes. Eosinophils were not seen during convulsions. There was also some variation in the red cell count. Guirdham and Pettit found no evidence of a daily leukocyte tide, either in subjects used as controls or in the epileptic patients.

KASANIN, Chicago.

SOME OBSERVATIONS ON MASKED EPILEPSY AND THE SIMULATION OF TRAUMATIC EPILEPSY BY CEREBRAL TUMOUR, WITH SPECIAL REFERENCE TO HEAD INJURIES WITHOUT FRACTURE. LEWIS R. YEALLAND, J. Neurol. & Psychopath. **16**:353 (April) 1936.

In cases of tumor of the brain epilepsy may develop after a minor injury to the head without fracture of the skull. Epilepsy in these cases may be classified into two groups: (1) traumatic epilepsy and (2) masked epilepsy. In the latter type, in addition to subjective symptoms common to trauma, recognition of epileptic fits is obscured by complete amnesia for the somatic experience, difficulty in describing the corticosensory experience or the sudden onset of hemiplegia. Because of the elasticity of the skull, injury to the head, even though insignificant, will cause sinking of the skull. This tends to diminish the intracranial capacity and to crush the brain as a whole. When a cerebral tumor also occupies the brain-containing space, injury to the head tends to crush the intracranial contents beyond the amount due to sinking of the skull. It may then act as a possible mechanical factor in precipitating the onset of epilepsy.

N. MALAMUD, Ann Arbor, Mich.

VON HIPPEL'S DISEASE; LINDAU'S DISEASE. H. VIALLEFONT, Rev. d'oto-neuro-opht. **13**:485 (July-Aug.) 1935.

In this article Viallefont discusses together von Hippel's disease and Lindau's disease. Retinal angiomatosis is rare and affects young persons (before the age of 25 years) by predilection. It is not congenital, however, and attacks the two sexes with equal frequency. The most striking factor in the etiology of the pure or associated form of angiomatosis is its familial and hereditary character. In the beginning it is unilateral, and a long interval intervenes before the second eye is involved. Visual acuity diminishes little by little and is accompanied by narrowing of the visual field, at times with scotoma. The eyeground has a pale

orange tint. Optic neuritis may occur early. In the manifest stage the subjective symptoms are more marked; examination of the eyegrounds reveals tortuous, dilated vessels in pairs, extending from the papilla to the periphery; intercalated in the circulatory circuit is a yellowish red, round, tumorous mass, which projects above the retinal surface. The eye may contain several such units as the disease evolves. Surrounding the masses are whitish patches (proliferation of benign character), which may mask the original lesion and extend to the maculopapillary region; they represent a glial reaction and are secondary to the angiomatous process. Complications include localized or profuse hemorrhages, detachment of the retina, glaucomatous attacks and choroidal cataract. The reticular proliferated cells are often attacked by xanthomatous or cystic degeneration. Extra-ocular lesions are observed in the nervous system, the cerebellum, the vicinity of the fourth ventricle, the bulb and the spinal cord. Lesions in the cerebellum are usually single. Histologically, the angiomatous tumor is formed by capillaries, among which are cells which Lindau, Cushing and Bailey stated to be of endothelial origin (angioreticuloma). When the intervascular cells are of glial origin, the tumor is called angioglioma. The angioreticuloma evolves by fibrous alteration of the reticular stroma, or by xanthomatous or cystic transformation. Visceral lesions are situated in the pancreas, kidneys and adrenal glands; they are cysts, the walls of which are formed by cuboidal or squamous cells of the endothelial type. Lesions of the liver, ovaries and bones have been observed. Many and varied theories of the pathogenesis of Lindau's and von Hippel's disease have been voiced. Viallefont confesses complete ignorance of the intimate pathogenic processes involved in pure or associated retinal angiomatosis.

DENNIS, San Diego, Calif.

TUMORS OF THE SELLAR REGION. D. MANOLESCO, D. LARESCO and G. SCHMITZER, Rev. d'oto-neuro-opht. **14**:553 (Sept.-Oct.) 1936.

The histories in two cases of sellar tumor confirm the previously expressed dicta of Manolesco, Laresco and Schmitzer, viz.: (1) the necessity of examining the visual field for color; (2) the test for light perception in the various zones of the visual field; (3) the examination of the visual field in oculomotor paralyses; (4) the obligation to use roentgenotherapy in all cases of tumor of the sellar region, and (5) the return after roentgenotherapy of the visual fields as separate islands.

In the first case exophthalmos was associated with the intrasellar syndrome. Uhthoff found this sign present in 8 per cent of a large number of cases which he studied. The authors think that this figure is too low. In their study of twenty-six cases exophthalmos was observed in 12.5 per cent. In the second case, in which the diagnosis was confirmed by the evolution of the disease and by giantism, polyuria, atrophy of the optic nerve and the roentgenogram, hemianopia was not present. Statistics furnished by the ophthalmologic clinic of Bucharest agree with Uhthoff's findings that hemianopia is absent in 5 per cent of cases of hypophysial tumor associated with acromegaly and in 20 per cent of those in which there is not acromegaly. Examination of the point of fixation revealed the presence of scotomas of the bitemporal, hemianopic type, which indicated a lesion of the chiasm. This finding was important because of the absence of modification of the peripheral fields. The conclusion is forced that there was a lesion of the papillomacular bundle in the chiasm, and the findings confirm the conception that these fibers lie ventrad in the posterior segment of the chiasm. Hence, a hypophysial tumor which compressed the chiasm from below upward would affect these fibers exclusively.

DENNIS, San Diego, Calif.

ANATOMIC EXPLANATION OF DYSARTHRIA ASSOCIATED WITH DEMENTIA PARALYTICA. R. OGINO, Psychiat. et neurol. jap. **39**:27 (Dec.) 1935.

Eight cases of dementia paralytica in which there was pronounced dysarthria were compared histologically with four cases used as controls in which slight or

no dysarthria was shown. All parts of the cortex, basal ganglia and brain stem were examined. It was observed that the cortex was much more seriously damaged in cases of severe dysarthria than in the cases used as controls. No special part of the cortex was more affected than others. The striatum was always severely damaged, except in the cases used as controls. Both the large and the small ganglion cells were diseased, and there was glial hyperplasia. Only mild changes were visible in the substantia nigra and the cerebellar nuclei. Minor changes were noted in the bulbar nuclei. Ogino denies the production of dysarthria by cortical involvement. He maintains that the striatal lesions are intimately connected with the dysarthria and postulates the theory that the striatum takes part in all articulatory elements—successive, simultaneous, musical and logoclonic.

ALPERS, Philadelphia.

Peripheral and Cranial Nerves

NEUROFIBROMA AND NEUROFIBROSARCOMA OF PERIPHERAL NERVES UNASSOCIATED WITH RECKLINGHAUSEN'S DISEASE: A REPORT OF TWENTY-FIVE CASES. ELLIOTT C. CUTLER and ROBERT E. GROSS, Arch. Surg. **33**:733 (Nov.) 1936.

Twenty-five representative cases of benign or malignant tumor of the sheath of a peripheral nerve, unassociated with Recklinghausen's disease, are reported. The most frequent sites for the neoplasm are the posterior surface of the legs and the anterior surface of the arms and neck. The tumor varies greatly in size and has a marked tendency to cystic degeneration. The benign form is easily separated from the nerve trunk, which can be left intact. The malignant tumor infiltrates and cannot be separated from the nerve. In dealing with a slowly growing neurofibroma, it is justifiable to peel it off from the nerve, but in case of a tumor showing a more rapid rate of growth, a portion of the nerve should also be resected, followed by end to end suture of the nerve. Operation on sarcoma of the nerve sheath should be radical, and in the absence of metastases early amputation of the involved limb gives the best chance of cure. Radium or roentgen irradiation of the malignant form has been almost universally a disappointing procedure.

GRANT, Philadelphia.

NEURALGIAS AND EAR SYMPTOMS, ASSOCIATED WITH DISTURBED FUNCTION OF THE TEMPOROMANDIBULAR JOINT. JAMES B. COSTEN, J. A. M. A. **107**:252 (July 25) 1936.

Costen, in a review of a large group of cases in which headache and aural symptoms were shown to be partially or altogether due to disturbed function of the mandibular joint, shows this to be a common factor. The pain and involvement of the ear are similar in every respect to those in some commonly known disorders of the eye, sinus and ear. Eighty-five patients fell into the group with pain, which included persons with burning and sensory disturbance about the tongue and pharynx. Four of these patients showed salivary disturbance, which may be traced directly to irritation of the chorda tympani and auriculotemporal nerves; these effects also were relieved. Thirty-five of the forty-two patients with aural symptoms presented varying grades of catarrhal deafness, due either to compression from overclosure or to chronic nasal infection. Four of the patients with aural disturbance presented shortened bone conduction and were not improved by reposition of the jaw; these may be regarded as having either eighth nerve deafness or microfracture of a region near the otic capsule which interfered with transmission of sound waves to the inner ear, as observed by Guild. The dizziness is not typical of toxic labyrinthitis. Twenty-six of the series of patients, or about 20 per cent, showed mild herpes of the buccal mucosa, the angles of the mouth and the external auditory canal, which in all cases was

preceded by pain and improved with disappearance of the other symptoms. The results of reposition of the jaws were generally good except in a few cases of malocclusion of natural teeth, in which great difficulty was presented. However, it was noted that the conditions showing the best results were corrected in several stages, by slowly increasing the vertical dimension of the jaw. This increase in distance is built into the molar district of the jaw and is not a problem merely of "opening the bit." Some failures to obtain a proper result have been traced to lack of understanding of this point and the anatomic problem involved by the dentist.

EDITOR'S ABSTRACT.

ETIOLOGY OF POLYNEURITIS IN THE ALCOHOL ADDICT. NORMAN JOLLIFFE and C. N. COLBERT, J. A. M. A. **107**:642 (Aug. 29) 1936.

Jolliffe and Colbert point out that vitamin deficiency may be an etiologic factor in the development of polyneuritis in the alcohol addict, first mentioned on theoretical grounds by Shattuck in 1928 and Minot in 1929. After reviewing the investigations carried on by other authors, they report their own investigations. The alcohol addict selected for this study had polyneuritis, as evidenced by symmetrical sensory changes in the peripheral nerve distribution of the lower extremities and, as a rule, by changes in the deep tendon reflexes. Patients having complications likely to increase the vitamin B requirement or to prevent absorption from the gastro-intestinal tract or utilization of vitamins (pneumonia, tuberculosis, hyperthyroidism, delirium, vomiting, diarrhea, pellagra, clinical icterus and ascites) were excluded from this study. Palpable liver, dependent edema, low grade fever, achlorhydria, anemia, anorexia or a psychosis not associated with delirium did not cause exclusion. The selected patients were placed in rotation into groups A, B and C until twenty-three subjects were studied; then five successive patients were placed in group C, making a total of twenty-eight subjects. Certain subjects in groups A and C, after observation in their respective groups, received treatment designed to test a therapeutic agent. All subjects were given physical therapy, and symptomatic treatment was given as occasion required. Group A: The seven patients in this group were given a basal diet estimated to contain 2,190 calories and 3,680 mg. equivalent (736 Sherman units) of vitamin B. The vitamin/calory ratio of this diet is 1.7, which shows borderline adequacy for subjects weighing from 58 to 63 Kg. Group B: The eight patients in this group received the same basal diet as those in group A, but in addition they were given 18 Gm. of unheated Vegex daily. Vegex contains about 225 mg. equivalent (45 Sherman units) of vitamin B per gram. This added 4,050 mg. equivalent of vitamin B to the basal diet, making the vitamin/calory ratio 3.6, showing double the vitamin B requirement of a subject weighing 64 Kg. Group C: The thirteen patients in this group received a vitamin-rich diet estimated to contain 3,100 calories and 17,250 mg. equivalent of vitamin B, resulting in a vitamin/calory ratio of 5.5. To this diet was added 18 Gm. of Vegex daily, bringing the vitamin/calory ratio up to 6.8. This ratio is almost twice that obtained for subjects in group B and four times that obtained for subjects in group A. The authors describe and discuss the results they obtained, and, in summarizing their observations, they state that those receiving borderline amounts of vitamin B showed no improvement in the objective signs of peripheral neuritis over a period of a month. Two of these subjects were then given crystalline vitamin B_1 by intravenous injection, with dramatic response in one and a good response in the other. Subjects treated with a vitamin B intake approximately twice their predicted requirement showed improvement, but not as rapidly or to the same degree as those receiving four times their vitamin B requirement. On the basis of the possibility of a fraction in the vitamin B complex other than the vitamin itself augmenting the action of vitamin B on polyneuritis in the alcohol addict, the authors have concluded: 1. Alcohol per se is not the cause of polyneuritis in the alcohol addict. 2. Vitamin B deficiency is a cause of polyneuritis in the alcohol addict.

EDITOR'S ABSTRACT.

GLOSSOPHARYNGEAL NEURALGIA. W. B. HOOVER and J. L. POPPEN, J. A. M. A. **107**:1015 (Sept. 26) 1936.

According to Hoover and Poppen, trigeminal and glossopharyngeal neuralgia are alike in all respects except the location of the agonizing flashes of pain and of the trigger areas which set off these paroxysms. The trigger areas in glossopharyngeal neuralgia include the pharyngeal wall, the tonsillar region, the base of the tongue and, rarely, the ear, while trigger areas in trigeminal neuralgia occur in the buccal mucous membrane and about the lips, nose and various areas of the face. When the first or second division of the trigeminal nerve is affected, there should be little or no difficulty in the differentiation of these two neuralgias, but when the third division is involved, more care must be exercised to differentiate this form from neuralgia of the ninth nerve. Cocainization of the mucous membranes over the distribution of the ninth nerve will, as a rule, control temporarily the paroxysmal pain from this nerve. Medical and surgical procedures are available in the treatment of glossopharyngeal neuralgia. In the authors' experience trichlorethylene has been the only drug really efficient in giving a marked amount of relief from this condition. It is administered by inhalation of from 15 to 30 drops from three to four times a day. The surgical treatment of choice is the intracranial section of the ninth nerve in the posterior fossa.

EDITOR'S ABSTRACT.

GASTROGENOUS POLYNEURITIS. A. H. DOUTHWAITE, Brit. M. J. **2**:535 (Sept. 12) 1936.

Douthwaite has studied seven patients with polyneuritis in whom the only constant feature was disturbance of gastric function; there was either reduction or absence of free hydrochloric acid. The current conception concerning achlorhydria and achylia is that in most cases this condition appears as the terminal result of chronic gastritis. When atrophy of the mucous membrane of the stomach and possibly of the first portion of the duodenum becomes complete, pernicious anemia and subacute combined degeneration are likely to arise, owing to absence of the as yet unidentified substance known as hemopoietin and neuropoietin. In some cases of subacute combined degeneration there is evidence of polyneuritis, and it seems reasonable to suspect that the health of the peripheral nerves is, like that of the spinal cord, dependent on an adequate supply of neuropoietin or of some allied substance secreted by the gastric and the duodenal mucosa.

In view of the cases observed, Douthwaite feels justified in postulating the possibility of the existence of gastrogenous polyneuritis. Three of the patients presented a slightly modified blood picture and were given therapy for anemia with hydrochloric acid; all improved within a few months and remained well; two had definite gastro-intestinal defects, correction of which resulted in cure. The other two patients had gastric carcinoma.

BECK, Buffalo.

ELEVEN CASES OF CONGENITAL MOTOR DISTURBANCES OF THE CRANIAL NERVES IN ONE FAMILY. A. H. FORTANIER and N. SPEIJER, Encéphale **31**:252, 1936.

The disease considered here was first described by Moebius as *infantiler Kernschwund* and was attributed to prenatal degeneration of the cranial nerve nuclei. Three types have been described, depending on the nerves involved. The first type involves only the territory of the oculomotor nerve, and the second, that of the facial nerve and sometimes the sensory or motor territory of the trigeminus nerve and/or the acoustic nerve. In only one case was there any disturbance of lacrimal secretion (Zappert). In the third type only the hypoglossus and glossopharyngeus nerves are involved. These disturbances are generally hereditary and seem to be dominant. In some cases other congenital anomalies, particularly spina bifida, are present. In some families there are also psychoses.

The family reported here consisted of sixty-eight persons. Information is given on five generations. Deafness was the only defect known in the first two genera-

tions—congenital deafness on one side and deafness following typhoid in the father and brother of the maternal progenitor, who was not herself deaf. Yet she, as well as her sister, who married a man with no known hereditary defect, had offspring with the disease. In four cases there were lacrimal disturbances. The other defects, which were present alone or in combination, were congenital facial paralysis, congenital deafness and spina bifida. There were no psychoses. In several patients examined there were only latent disturbances of the motor nerves, such as excessive sensitivity of the trunk of the facial nerve to galvanic stimulation. There were no known psychoses. The factor of heredity is certain in this family. The mode of transmission can be explained only as that of an irregular dominant trait; that is, in some persons the trait is recessive. This would explain, among other things, the presence of latent disturbances, revealed only by electrical examination. One member of the last generation, in addition to congenital bilateral facial palsy, deafness and absence of lacrimal secretion, presented excessive brachycephaly, epicanthus, deviation of the little finger and congenital paralysis of both lower extremities, which, however, improved with age. The intellect was normal. The motor disturbances may perhaps be considered as an abortive form of Oppenheim's amyotonia congenita. The heredity is obscure in this case.

LIBER, New York.

OPHTHALMIC HERPES ZOSTER AND TOTAL PARALYSIS OF THE OCULOMOTOR NERVE. P. NICOLAU and S. DRAGANESCO, Rev. d'oto-neuro-opht. **14**:479 (July-Aug.) 1936.

A woman aged 52, five days after contusion of the left frontoparietal region, experienced suborbital and ocular neuralgia. On the following day a vesicular eruption appeared in the left frontal region and the left upper eyelid. Two days later vesicles appeared on the outer limb of the cornea and the left nasal ala. Mydriasis with loss of the light reflex and ptosis accompanied the eruption. Paralysis of the third nerve became total four days later. Superficial keratitis with cyclitis occurred after another five days. Regression began only after five weeks, and three months after onset of the illness, slight ptosis of the left lid, slowness of pupillary reaction to light and residual keratitis were still present. The fact that the cerebrospinal fluid showed no albuminocytologic changes indicates that the infectious process was confined strictly to the nerve pathways and that when the meninges were reached immunization had already occurred. In 1922 Marinesco and Draganesco advanced the theory that the zosterian vesicle is an ectodermal reaction process, due to intradermo-epidermal penetration of a filtrable virus and not to trophic disturbances. Nuclear and protoplasmic inclusions in the cells removed from the vesicular area and the presence of infiltrative alterations in the subjacent derma and nerve terminals were demonstrated. The propagation of the virus along preformed nerve pathways was called odogenesis by Marinesco and Draganesco, whether ascending (neuroprobasis of Levaditi), descending (Foerster) or by diffusion along all cerebrospinal and sympathetic nerve conductors (septineuritis of Nicolau). According to Levaditi, the portal of entry of the zonal virus is the rhinopharynx, while Marinesco and Draganesco expressed the belief that the infection is cutaneous. Local factors—modifications of the physicochemical properties of the skin—probably influence the localization of the infectious process. The course of the virus in the case reported was along the frontal nerve to the gasserian ganglion, thence to the nasal nerve, the ophthalmic ganglion, the long ciliary nerves and the third nerve, via the motor root of this nerve to the ophthalmic ganglion. The appearance of the eruption in stages is proof that the zonal virus followed preexisting nerve pathways, its propagation being directed by its neurotropic affinity and by odogenesis.

DENNIS, San Diego, Calif.

Treatment, Neurosurgery

LIVER THERAPY FOR COMBINED SCLEROSIS. WALTER F. SCHALLER and HENRY W. NEWMAN, Arch. Int. Med. **58**:45 (July) 1936.

Adequate liver treatment is effective in the arrest and improvement of the neurologic manifestations of pernicious anemia, according to the experience of Schaller and Newman. Most unfavorable reports represent cases in which the parenteral injection of liver extract has been employed inadequately or not at all. The authors review forty cases and find that adequate therapy was sustained in only eight. The determinant of the adequacy is a dose of liver extract sufficient to maintain a red cell count in excess of 4,000,000. When the erythrocyte index falls below this, the dose of liver extract must be raised to elevate the red cell count to the desired level. In six of the eight cases it was necessary to use parenteral treatment with the extract; in the other two instances administration of liver by mouth seemed effective. Use of liver extract by injection is more potent than by oral ingestion, and administration by the latter method is more satisfactory than the eating of whole liver. Ideally, however, both whole liver and the extract should be used simultaneously, the doses being adjusted according to the effect on the red cell count. If the red cell count is maintained in excess of 4,000,000 but the neurologic status remains unimproved, the dose of the extract to be injected should be increased. In adequately treated patients in this series there was no record of any aggravation of neurologic findings.

DAVIDSON, Newark, N. J.

OPERATIVE EXPERIENCE IN CASES OF PINEAL TUMOR. WALTER E. DANDY, Arch. Surg. **33**:19 (July) 1936.

Three patients survived presumably total extirpation of tumor of the pineal body. One patient died three months later; in the second patient the tumor recurred in two and one-half years, and the third patient is living and apparently well, four months after operation. In most cases pineal tumor causes only signs and symptoms of intracranial pressure, due to occlusion of the aqueduct of Sylvius. Important localizing signs occurring at times are ptosis, usually bilateral, limitation of the upward movements of the eyes and fixation and dilatation of the pupils. In none of the ten cases were there any endocrine disturbances. Perhaps the most important objective evidence of a pineal tumor in young children—but not in adults—is a calcified shadow. Precise localization in all cases of pineal tumor can be made by ventriculography. The pathognomonic changes are a filling defect in the posterior part of the third ventricle and obliteration of the suprapineal recess. Six (60 per cent) of the ten tumors in this series were in children between 10 and 17 years of age. The weights of the tumors ranged from 3 to 18 Gm.

A pineal tumor is exposed by an occipital approach, with separation of the right cerebral hemisphere from the falx and splitting of the corpus callosum. In case of a large tumor in which the ventricles are small, resection of the posterior part of the right cerebral hemisphere is necessary. This method was used in four cases, in three of which the outcome was fatal and in one successful. Transient blindness and subtotal paralysis of all the extra-ocular muscles followed operation in each of the three cases in which intervention was successful. These disturbances disappeared a week or ten days later. They were doubtless due to edema resulting from trauma to the quadrigeminal plate, in which the tumor is always firmly embedded, and to the underlying brain stem. Left homonymous hemianopia may or may not follow and be permanent. It is probably due to compression of the cuneus during the separation of the hemisphere at operation.

GRANT, Philadelphia.

REMARKS ON EFFECTS OF ROENTGEN THERAPY UPON GLIOMAS. E. M. DEERY, Bull. Neurol. Inst. New York **4**:572, 1936.

Surgical intervention followed by roentgenotherapy is the approved method of treatment for glioma, although a precise knowledge of all the effects of irradiation is lacking. Deery reports the results of a study of fifty cases of glioma, in an effort to determine the effects of irradiation by comparative examination of specimens of tumor tissue before and after irradiation. The group included examples of all the currently recognized types of glioma, but the majority were medulloblastoma, glioblastoma and astrocytoma.

The tissue changes following irradiation seemed to be due to the direct action of radiation on the tumor cells. Some tumors of each cell type showed changes which were attributed to irradiation; others, only moderate change, and still others, no change. The cell changes were: (1) evidence of cell injury sufficient to cause cell death, increase of necrosis and appreciable reduction in the cellularity of the growth as determined by actual cell counts; (2) reduction of mitotic figures, and (3) increase in the number of giant cell forms. Phenomena associated with the blood vessels and connective tissue which are commonly seen in material after irradiation are considered as secondary and essentially incidental changes.

Deery believes that attempts to determine the relative sensitiveness of the various types of glioma to roentgenotherapy require a greater volume of material than one clinic can supply. He proposes the pooling of cases from many clinics for correlated studies of histopathologic changes, period of survival dosage, classification and standardization of the evaluation of malignancy.

KUBITSCHEK, St. Louis.

THE HYPOGLYCEMIC STATE IN THE TREATMENT OF SCHIZOPHRENIA. BERNARD GLUECK, J. A. M. A. **107**:1029 (Sept. 26) 1936.

Glueck states that the evidence is far from conclusive that the effects of the hypoglycemic state and the insulin shock in patients with schizophrenia are specific to this form of disorder. The average patient's reaction to this sudden deprivation of the organism of its sugar content has much of the nature of a profound organismal and personality disintegration. No other form of psychiatric therapy requires as much care, skill and caution in its application as this. Four deaths have been recorded in connection with the treatment—three in Vienna and one in Switzerland—but it is impossible to state with accuracy what percentage these constitute of the total number of patients treated. While undergoing the treatment, the patients appear to be in fine physical condition; they usually gain weight and, aside from a slight sense of fatigue, do not complain of physical discomfort during the time that they are not in the hypoglycemic state. The object is to achieve progressive insulinization of the patient through the intramuscular administration of daily increasing doses of insulin until the so-called shock dose is attained.

EDITOR'S ABSTRACT.

TREATMENT OF INTRASELLAR TUMOURS BY RADON. W. O. LODGE, Brit. M. J. **2**:1257 (Dec. 19) 1936.

The method of implanting radon seeds by means of the orbitonasal route is easy and in selected cases may prove more effective than an abortive attempt to remove either a very large or a malignant tumor. The appearance in a roentgenogram of the calcified wall of a suprasellar cyst is a contraindication to radium therapy; one must also make careful selection in cases of a large intrasellar growth. If the sella turcica has been so distended as to reduce to a shell the body of the sphenoid bone, surgical access can be obtained by displacing the orbital fascia and contents outward and removing the ethmoid cells. Radon seeds can then be inserted without difficulty. In order to avoid the angular vein and permit bilateral access, if necessary, a medial interorbital incision is recommended.

BECK, Buffalo.

PHARMACOLOGIC STUDIES OF THE BASIC FACTORS INVOLVED IN THE TREATMENT OF EPILEPSY WITH BORATES. C. MAIER, Monatschr. f. Psychiat. u. Neurol. **91**:41 (April) 1935.

According to Maier, borates are of definite benefit in treatment for epilepsy. They are useful in treating patients who react unfavorably to bromide and phenobarbital. An advantage of this therapy is that it does not produce narcotic effects. It may be employed with benefit in conjunction with bromide or phenobarbital. Sodium borotartrate and other borotartrates, in doses of from 8 to 14 Gm. daily, are recommended. Experimental studies made by Maier showed that the administration of preparations of borates to animals abolishes or favorably influences convulsions produced by picrotoxin and betatetrahydroxynaphthylamine. In contrast to the effect of bromide, borate therapy is not associated with change in the chloride content of the blood. It was found that borate tends to produce slight acidosis and that it inhibits the swelling of gelatin to a greater extent than any of the substances included in the Hofmeister series. These effects, which explain the diuresis and loss of weight frequently observed in patients to whom borate is administered, are responsible for the success of the treatment.

ROTHSCHILD, Foxborough, Mass.

TREATMENT OF SCHIZOPHRENIA BY PRODUCTION OF A HYPOGLYCEMIC STATE. G. LANGFELDT, Psychiat.-neurol. Wchnschr. **38**:483 (Sept. 19) 1936.

Langfeldt treated eight patients with schizophrenia by insulin shock. The results were discouraging. In only one case was there a good remission. The treatment endangered the life of the patients and was discontinued.

BRUETSCH, Indianapolis.

Special Senses

FUNCTIONAL DISTURBANCES OF THE EYES. A. BIELSCHOWSKY, Arch. Ophth. **15**: 589 (April) 1936.

This paper, which is a continuation of Bielschowsky's recent general course in oculomotor disturbances, discusses the functional disturbances of the eye which may be caused either by anomalies of the dioptric or of the motor apparatus or by anomalies the nature of which is not yet known. That there is a casual connection between the subjective disorders and the anomalies which he discusses is evidenced by the frequent disappearance of the symptoms after correction of the anomalies. One of the characteristics in cases of these disorders is the similarity of the subjective symptoms of which patients with different anomalies complain. The history, then, obtained from the patient is important. Since many of these patients have a neuropathic constitution, an inherited disposition should be sought.

In his discussion of heterophoria, Bielschowsky calls attention to the advisability of testing the motor apparatus, regardless of the disorder for which the patient consults the ophthalmologist. It seems practically impossible to eliminate all types of innervation which influence the position of the eyes. Even in sleep or in deep narcosis there are almost constant movements of the eyes in parallel, opposite, lateral or vertical directions. Voluntary movement can be eliminated by ordering the patient to look straight forward at a distant point during a test, while any hyperopia causing possible accommodative effort which might involve the convergence innervation is corrected. By eliminating the movements of the head and body, the vestibular innervation, based on the connections between the vestibular and the oculomotor centers, can also be eliminated. There are other types of innervation which have nothing to do with the fusion apparatus and which change the position of the eyes at irregular intervals. One type produces either unilateral or bilateral dissociated vertical movements. Bielschowsky thinks that this condition, spoken of as double hyperphoria, is of purely nervous origin and that it does not belong to the true heterophorias. It is possible that this condition may be associated with some other latent or manifest horizontal deviation, but the condition itself is

not a surgical problem. To make the best possible use of duction power tests in the investigation of heterophoria and to avoid mistakes, one must remember that all types of innervation governed by the will as well as by the fusion apparatus are without exception equal in the two eyes. This law, which was formulated by Hering, has been substantiated by clinical experience. Some writers have doubted its truth and have cited the fact that some persons can move one eye alone or the two eyes unequally. These authors did not take into consideration that unilateral or unequal movement of the eyes must occur if two impulses are sent at the same time to the two eyes, as happens when while the eyes are directed to a distant point, another point nearer and to the left of the first attracts the attention. Then two types of innervation are required: one for convergence and the other for turning the eyes to the left. Both impulses drive the right eye to the left, whereas the left eye is driven to the right by the convergence impulse and, simultaneously, to the left by the levoversion impulse. The result must be that the left eye, in spite of having the same innervation as the right, will move less than the right, or not at all.

In considering heterophoria of paretic origin, Bielschowsky calls attention to the diagnosis and treatment of anisophoria, which Friedenwald defined as the form of heterophoria in which the degree of muscular imbalance of the eyes varies with the direction of gaze. Friedenwald divided this anomaly into two general classes: heterophoria of paretic origin and that produced by the correction of anisometropia with lenses with different peripheral prismatic effects for the two eyes. The first of these types is a problem of fusion training. The second is a matter of accurate optical correction of the anisophoria by a meniscus lens of no dioptric power, showing a peripheral prismatic action which increases regularly with the eccentricity of the gaze, the thickness of the lens and the depth of the meniscus.

In attempting to separate anisophoria from ordinary heterophoria, the main difficulties to be overcome are (1) the resistance of the compensating fusion innervation and (2) the unsteadiness of the latent deviation, even after almost complete relaxation of the fusion innervation by means of a duction power test. A greater or smaller fraction of that innervation frequently returns, even if fusion stimuli are excluded in the examination following the duction power test. This fraction of innervation is not constant but varies in an incalculable way, so that the deviation may appear now as a slight increase and now as a decrease and may induce misinterpretation, unless repetitions of the test disclose the unsteadiness of the deviation.

In many cases the patient obtains relief only after the aniseikonia has been found and corrected. Bielschowsky states that he has seen and examined some of the patients before and after the aniseikonia was corrected and that he found the amount of heterophoria to be almost unaltered by the iseikonic lenses. This proved to his satisfaction that not heterophoria but aniseikonia had caused the trouble and that the influence of iseikonic lenses on heterophoria is not as great as might be expected from a theoretical standpoint, considering the peripheral prismatic action of such glasses.

SPAETH, Philadelphia.

HOMONYMOUS HEMIANOPIA: PRACTICAL POINTS IN INTERPRETATION, WITH REPORT OF FORTY-NINE CASES IN WHICH THE LESION IN THE BRAIN WAS VERIFIED. THOMAS H. JOHNSON, Arch. Ophth. **15**:604 (April) 1936.

It has long been known that changes in the visual fields may supply important information concerning the location of a lesion of the brain. This study had two objects: (1) to determine to what extent homonymous hemianopia, when correlated with other symptoms of tumor of the brain, could be used to localize the growth more specifically and (2) to determine whether the various grades of homonymous hemianopia, such as quadrantic and sectoral defects, could be shown to have specific localizing values.

Anatomically, the lesions in the forty-nine cases were localized as follows: frontal and frontoparietal lobe, five cases; temporal lobe, twenty cases; temporal lobe but extending into the adjoining lobes, eight cases; pituitary gland, one case;

porencephaly and degeneration of the parietotemporal lobes, three cases; angioma of the right side of the tegmentum, one case, and tumor of the occipital lobe or primarily originating in the occipital lobe and invading the adjoining lobes, eleven cases.

In discussing tumor of the frontal lobe, Johnson calls attention to the fact that a tumor may exist in the frontal lobe for a long time without localizing symptoms. He found that a tumor at the base of the frontal lobe in the early stage may produce symptoms of retrobulbar neuritis, accompanied by a central or paracentral scotoma in the ipsilateral visual field. Exophthalmos is common in cases of meningioma of this lobe.

In Johnson's experience the syndrome of ipsilateral atrophy of the optic nerve with contralateral papilledema is not uncommon in cases of tumor of the frontal lobe. He thinks it probable that only a tumor at the base of the frontal lobe produces the characteristic changes in the optic nerve heads. Field changes are common in cases of tumor at the base of the frontal lobe, i. e., at the inferior portion of the lobe. When the pressure is exerted not directly on the visual structures but on areas adjacent to them, the change is likely to consist of a central scotoma in the ipsilateral field. Pressure confined to the optic tract produces contralateral homonymous hemianopia, which is likely to be complete in the proportion of 4:1 of the cases.

Tumor of the temporal lobe was seen in twenty-eight cases. In twenty instances the lesion was limited practically to the temporal lobe, and in eight the contiguous lobes were invaded. Homonymous hemianopia was complete in seven cases and incomplete in twenty-one. In three of the cases of incomplete hemianopia the defects were quadrantic and in seven crescentic. Johnson quotes Cushing in expressing the belief that a lesion situated in the posterior part of the temporal lobe is less likely to produce partial defects in the fields, or to be detected, than one that involves the optic radiations in the anterior segment of the lobe. Hence, the optic radiations, as they occupy a considerable portion of each lobe, are expected to, and do, supply the most important localizing evidence when they are implicated by the resulting homonymous hemianopic changes in the visual fields, the incomplete defects being particularly characteristic. Visual hallucinations, consisting of scenes and panoramas due to irritation of the optic radiation, are diagnostic of tumor of the temporal lobe.

Ten cases of tumor of the occipital lobe were studied. In four cases the tumor was confined to the occipital lobe; in five it extended to the parietal lobe, and in one, to both the parietal and the temporal lobe.

Homonymous hemianopia follows implication of the visual center. In the beginning the field defect may be quadrantic, progressing to complete half-blindness as the growth increases. Rarely, a tumor in the midline affects both calcarine areas, causing bilateral homonymous hemianopia. Visual hallucinations, consisting of flashes of light and spectroscopic luminosities, are significant of invasion of the occipital lobe.

Johnson says that hemianopia is much more frequent in tumor of the temporal lobe than in tumor of the occipital lobe, for tumor of the occipital lobe is relatively much less common. On the other hand, homonymous hemianopia, when found, is more likely to be complete than incomplete in tumor of the occipital lobe.

Johnson states that crescentic defects in the visual fields are not as significant of tumor of the occipital as of tumor of the temporal lobe, that they are as frequent as quadrisectoral defects in cases of tumor of the temporal lobe, that central vision in homonymous hemianopia is retained, as a rule, until secondary atrophy of the optic nerve has resulted from concomitant papilledema, that a homonymous field defect of the slightest degree accompanied by papilledema is strongly significant of tumor of the brain, that encephalography or ventriculography is indicated in any case of an obscure neurologic lesion with a progressive hemianopic field defect, particularly if papilledema is present, and that homonymous hemianopia does not represent involvement of any specific area of the brain. The lesion may be in the visual system at any site posterior to the optic chiasm.

SPAETH, Philadelphia.

ISOLATED ELECTRIC STIMULATION OF THE TWO VESTIBULAR NERVES: DOUBLE CHRONAXIA ON EACH SIDE. G. BOURGUIGNON, Rev. d'oto-neuro-opht. **13**:781 (Dec.) 1935.

It has long been known that excitation of a single exposed semicircular canal in the pigeon by the use of bipolar electrodes produces an inclination of the head to the right or to the left, depending on the direction of the current. Bourguignon attempted isolated stimulation of one labyrinth in man by applying one small electrode in the ear and another to the mastoid of the same side. With the positive pole in the ear the head was inclined toward the side stimulated; with the negative pole in the ear the inclination of the head was toward the opposite side. In a subject in whom the eighth nerve on one side had been divided, no inclination of the head was obtained when the poles of the current were applied to the ear on that side; bipolar stimulation of the intact ear produced inclination of the head in one of the two directions, according to the direction of the current: stimulation with the positive pole in the ear produced the same vestibular chronaxia as binaural excitation with the positive pole on the sound side; the stimulation with the negative pole in the ear caused the same chronaxia as binaural excitation with the positive pole on the side of the sectioned nerve, indicating that stimulation was from the negative pole on the sound side.

In a normal man the chronaxia, measured by the bipolar method (positive pole in the ear), is the same as that observed with the classic binaural stimulation; with the negative pole in the ear the chronaxia is from 10 to 20 per cent greater or less (depending on the subject) than that obtained by the classic method of binaural stimulation. "In man and in cats the vestibular chronaxias of the two ears are symmetrical in relation to the direction of the current, while in the rabbit they are symmetrical in relation to the direction of the stimulation." This difference is due to the different disposition of the eyes in the two groups: Man and the cat have binocular vision, and the rabbit has monocular vision.

DENNIS, San Diego, Calif.

THE POINTING TEST. WILHELM BEHRMAN, Upsala läkaref. förh. **42**:67 (July) 1936.

This extensive investigation deals with the clinical value of the pointing test. Behrman believes that contradictory reports and opinons are due to the fact that no standard methods of testing are used. In addition, there exists no accord among clinicians regarding the value of the pointing test as a clinical method. The difficulty lies also in the fact that no attempt has been made to ascertain the range of average deviations in the performance of the tests in normal persons. Behrman states that since there is no way of telling how far a person will past-point without stimulation, it is hard to determine whether the same person will point differently with stimulation.

In order to secure some notion concerning the range of normal variability, Behrman made use of statistical methods. He established first the average effect of a given type of stimulation in a number of normal persons and then the constancy of the effect of a given stimulation in an individual case. His investigation of spontaneous pointing in normal persons leads him to believe that the results are determined by the methods used. He tried eleven modifications of the original technic of Bárány. One is a corrected pointing test, with the subject's head bent backward and one arm moving downward toward a table, the top of which is replaced by a plate of glass. Another method is uncorrected upward pointing toward the plate, and the third method, uncorrected upward pointing with both arms toward the plate. The glass was fitted into a table top for visibility and recording. Behrman found that in upward movement toward the goal there was drifting of the arms from the midline outward. In the third method there was an average deviation of 3.79 ± 0.08 (0.25) cm. for the right arm and 3.33 ± 0.08 (0.25) cm. for the left. With other methods in which the goal is reached by a downward movement, no definite outward deviation, or only deviations inward,

were noted. Behrman therefore comes to the conclusion that the general view according to which the arms always have a tendency to deviate spontaneously outward is erroneous.

He found further that in pointing tests in which correction toward the goal is made there is a mild range of variation of from about 10 to 15 cm., while in uncorrected methods the variation is twice as large. He also observed that methods with the tendency for spontaneous past pointing outward show an increase in past pointing for the right arm and none for the left.

Study of the average effects of stimulation showed that past pointing takes place invariably in the direction established by Bárány and other investigators. After caloric stimulation or rotation past pointing is in the direction of the slow phase of the nystagmus. When the head is turned deviation is in the opposite direction, and when the head is bent, deviation is in the same direction. The degree of deviation following stimulation depends on the methods used; it is greater when tests are used which require upward movements of the arms, especially when no correction is made after each pointing. This effect is more pronounced when the person tested points with both arms simultaneously. Behrman found further that after calorization deviation of spontaneous pointing from the range of the normal average increases slowly, reaches its maximum at about the tenth pointing and decreases gradually from then on. As an example, he offers the following observation: The effect of stimulation following rinsing the left ear with 100 cc. of water at a temperature of 20 C. was 5.22 ± 0.56 cm. for the right arm at the first pointing, while at the tenth pointing it increased to 11.66 ± 0.81 cm. The corresponding figures for the left arm were 2.71 ± 0.62 cm. and 7.97 ± 0.79 cm., respectively. After rotation the type of deviation was entirely different. The greatest deviation was at the first pointing and decreased in the subsequent tests. The effect following rotation to the right was 9.93 ± 0.87 cm. for the right arm at the first pointing and 3.82 ± 0.74 cm. at the second trial. The corresponding figures for the left arm were 9.03 ± 0.88 cm. and 4.91 ± 0.74 cm., respectively.

Behrman claims that the method of testing determines which arm will show the greatest reaction to a definite vestibular stimulation. One method may produce the greatest influence on the homolateral arm, and another method, on the contralateral. He found that rinsing the ear with cold water affects chiefly the opposite arm, while rinsing with warm water affects the homolateral arm. Rotation has its greatest effect on the arm which is opposite the direction of rotation. All these observations are formulated in a rule according to which in the test of pointing the strongest reaction following rotation or calorization will be in the arm which must deviate mesially when it deviates in the direction of the slow component of nystagmus. Rinsing with large quantities of water (100 cc.) produces stronger reactions than rinsing with small quantities; stronger reactions are also obtained with cold water. Behrman concludes that the diagnostic value of the pointing test is enhanced through the use of repeated stimulation tests in the same person. He showed further that the range of variation of pointing increases considerably after stimulation. Occasionally this range of variation is twice as large after stimulation as that in spontaneous pointing. Behrman was unable to establish any definite relationship between the onset of dizziness and the degree of past pointing. No relationship could be established between the direction of the apparent movement and that of the deviation.

NOTKIN, Poughkeepsie, N. Y.

Society Transactions

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, March 19, 1937

J. W. McCONNELL, M.D., *President, in the Chair*

PROGRESSIVE PARALYSIS OF THE DORSAL INTEROSSEOUS NERVE. DR. ALEXANDER SILVERSTEIN.

Paralysis restricted to the distribution of the deep branch of the radial or the posterior interosseous nerve is uncommon; when first encountered, it may prove confusing and be mistaken for chronic disease of the cells of the anterior horn. In the literature little mention is made of this condition. Woltman and Learmonth (*Brain* **57**:25, 1934) collected 9 cases, in the majority of which the condition was due to direct trauma to the nerve. In 1 of their 5 additional cases, exploratory operation revealed an anatomic anomaly of the nerve; they expressed the belief that the anomaly could account for the etiology in that particular case. In the 4 other cases the patients refused operation.

REPORT OF CASE

V. C., a salesman aged 30, entered the Temple University Hospital on Dec. 7, 1936, in the service of Dr. Temple Fay, with the chief complaint of weakness of the right hand. The past and the family histories were without significance. The patient had never been in contact with lead. For several years prior to onset of the condition his work required the use of an old typewriter which, he said, caused overexertion of his fingers. He also played the violin several hours a day at this time. The present disability began six years previously with weakness in the small finger of the right hand while typing. The condition progressed gradually until the other fingers were affected and reached its present state after several months. Shortly after the onset there appeared progressive wasting of the muscles of the back of the forearm. In November 1936, there appeared sudden spasms or jerking of the affected upper limb when it was relaxed.

Examination disclosed impairment of extension at the wrist and paralysis of the extensor muscles of the fingers. Extension of the thumb was lost completely. There was marked atrophy of the extensor muscles of the dorsum of the forearm. The electrical reactions showed complete reaction of degeneration in the extensor digitorum communis, extensor minimi digiti, extensor pollicis longus, abductor pollicis longus, extensor carpi ulnaris and extensor indicis muscles.

Laboratory examinations, such as the blood count, urinalysis, the Wassermann test and studies of the spinal fluid gave results within normal limits. Roentgenograms of the right upper extremity, including the shoulder, revealed nothing abnormal.

Comment.—The symptoms in this case, as in those reported by Woltman and Learmonth, began with weakness of extension of the fifth finger and extended radiad to involve the muscles supplied by the posterior interosseous nerve. The spasmodic jerking of the nonparalyzed muscles of the affected limb is difficult to explain. It may have been due to the unusual strain placed on these muscles to compensate for paralysis of the extensor muscles. The etiology is not determined. The patient's occupation, necessitating straining the fingers in typing, and playing the violin may have had some bearing. From cases reported in the literature

and from 3 observed personally, it would appear that movement from pronation to supination when long continued is an important factor. There may be some anatomic anomaly, such as that in the case of Woltman and Learmonth, in which the nerve was superficial to, instead of passing through the substance of, the supinator radii brevis muscle.

The characteristic clinical picture in the syndrome is (1) complete paralysis of the extensor muscles of the fingers of the first phalanx; (2) comparatively mild weakness in the extensor muscles of the wrist; (3) paralysis of the extensor muscles of the thumb, and (4) atrophy of the dorsum of the forearm.

DISCUSSION

DR. ERNEST SPIEGEL: Can an associated lesion of the ulnar nerve be excluded? I have the impression that spreading of the fingers is definitely weaker on the diseased side, indicating a lesion of the ulnar nerve.

DR. ALEXANDER SILVERSTEIN: The question raised by Dr. Spiegel was studied carefully. When the hand was supported dorsally at the metacarpal articulation and the first phalanx, the patient was able to perform movements of abduction and adduction of the fingers.

RELATION OF INCREASED INTRACRANIAL TENSION TO ARTERIAL HYPERTENSION. DR. EVELYN SCOTT.

Clinical observations are submitted supporting experimental evidence that increased intracranial tension may produce elevation of the systemic blood pressure. These determinations were made in a case in which there was no question of increase in intracranial tension with elevation of blood pressure, such as is observed in fracture of the skull or with an expanding cerebral neoplasm. Experimental evidence to this effect has been reported by Cushing, Raab and Cannon and has been reaffirmed within the past year by Schmidt and Forbes. Cushing produced an increase in intracranial tension in dogs by the introduction into the subarachnoid space of a physiologic solution of sodium chloride by a cannula passed through a trephine opening in the arch of the atlas. He found that the intracranial pressure can be increased to the point of equalizing the systemic blood pressure before sympathetic medullary symptoms of compensatory elevation of blood pressure develop. Beyond this point, elevation of blood pressure occurs, until the systemic pressure equals the intracranial. Interpreted clinically, this observation suggests that elevation of blood pressure is always compensatory to increase in intracranial pressure. That failure to compensate for increasing intracranial pressure by elevation of blood pressure occurs after cocainization of the medulla is proof that the mechanisms for elevation of the blood pressure are mediated through the autonomic system. Cushing expressed the belief that the basis of the increase in intracranial tension is venous stasis in the medullary areas.

Raab, working on this hypothesis, reproduced many clinical features of essential hypertension by means of duplicating experimentally the chemical conditions incident to stasis. He showed that lack of oxygen causes accumulation of lactic acid in the tissues. On perfusing the medulla of decerebrate cats with lactic acid through a cannula in the right carotid artery, he observed prolonged elevation in blood pressure. In such perfused cats the effects of inhalation of carbon dioxide, as shown by elevation of blood pressure, are greater than those in normal animals. In other words, the animals in which he produced conditions corresponding to those present in cerebral stasis showed the same sensitivity to accumulation of carbon dioxide through its effect on blood pressure as are seen in clinical cases of essential hypertension.

In a brain in which intracranial tension is increased there is plugging of the foramen magnum by the cerebellar tonsils with consequent pressure on the branches of the posterior inferior cerebellar artery, which supply the structures on the floor of the fourth ventricle.

In connection with the experimental work of Cushing and Raab, the following case is described. The outstanding feature was hypertension, apparently of long standing, since there were hypertrophy of the left ventricle and myocardial degeneration without arteriosclerosis or nephrosclerosis. In addition, there was compression of the medulla due to mechanical narrowing of the foramen magnum, resulting from Paget's disease.

A white woman aged 60 had been well until the age of 57, when she complained of headache and change in her features. At the Walter Reed Hospital the diagnosis of Paget's disease involving the skull and long bones was made. When admitted to the Philadelphia General Hospital in October 1935 (in the

Twenty-Eight Cases of Increased Intracranial Pressure in Which Hypertension Was Shown in the Absence of Visceral Disease *

Patients	Age, Years	Sex	Blood Pressure, Mm. of Mercury	Type of Cardiac Hypertrophy	Type of Increased Intracranial Pressure
Number under	6	M	160/120	Myocardial degeneration	Chronic
20 years, 7	11	M	150/ 80	Myocardial degeneration	Chronic
	12	M	160/ 85	Myocardial degeneration	Acute
	12	F	140/ 70	Myocardial degeneration	Chronic
	16	F	110/ 65 (T)	Left ventricle	Chronic
	17	F	170/125	None	Acute
	19	M	150/120	Left ventricle	Chronic
Number under	20	M	140/110	None	Acute
30 years, 7	20	F	150/ 0	Fatty degeneration	Acute
	21	M	180/108	Left ventricle	Chronic
	27	M	79/ 50 (T)	Left ventricle	Chronic
	28	M	140/130 (T)	Myocardial degeneration; dilatation	Acute
	29	F	180/ 60	None	Acute
	29	M	138/ 65 (T)	Concentric	Chronic
Number under	30	M	130/ 90	Left ventricle	Chronic
40 years, 7	30	M	.....	Concentric	Chronic
	32	F	130/100	Left ventricle	Chronic
	33	F	.....	Concentric	Chronic
	35	M	142/ 90 (T)	Myocardial degeneration	Acute
	38	M	.....	Concentric	Chronic
	38	M	170/100	Left ventricle	Chronic
Number under	43	M	120/ 75 (T)	Left ventricle	Chronic
50 years, 5	43	M	180/100	Left ventricle	Chronic
	45	M	140/ 90 (T)	Concentric	Chronic
	47	F	150/ 94	None	Acute
	47	F	148/106	Concentric	Chronic
Number under	52	M	160/ 90	None	Acute
60 years, 2	54	M	160/ 76	Left ventricle	Chronic

* The criteria of hypertension were elevation of blood pressure and cardiac hypertrophy.

service of Dr. William Drayton Jr.), she was becoming progressively weaker and had been confined to bed for six months. Mental examination showed irritability, retardation, impairment of memory, lack of insight and general apathy.

Physically, the patient appeared to be in a toxic state, and was dyspneic and somnolent. Her head was of unusual shape, with the transverse diameter considerably larger than the anteroposterior. There was marked exophthalmos of both eyes; the thyroid gland was not palpable; the heart was slightly enlarged to the left, with no murmurs; the rate was 130 and the rhythm was normal. The blood pressure was 180 systolic and 100 diastolic. The radial vessels were not palpable. There was pitting edema of both legs. The tendon reflexes were equal and active. The laboratory findings were essentially normal.

The course in the hospital was rapidly downward. Six days after her admission the patient became cyanotic, and the dyspnea increased; the temperature rose to 100 F. Two days later she was moribund. At this time the blood pressure was 90 systolic and 55 diastolic. She died the next day.

The clinical diagnosis was: senile psychosis, hypertensive arteriosclerotic cardiovascular disease with congestive heart failure, Paget's disease and terminal bronchopneumonia.

Postmortem examination confirmed the diagnosis of Paget's disease. The bones of the skull could be cut easily with a saw and showed the microscopic picture of osteitis deformans. Measurements of the skull showed: biparietal diameter (above the ears) 15.5 cm.; outside diameter of the foramen magnum 5.5 cm. and inside diameter 4 cm. The skull was thickest in the frontal region, where it measured 1.8 cm. The blood vessels, including the aorta, were free from arteriosclerotic changes. There were a mild degree of early sclerosis in the small pulmonary vessels and hypertrophy of the left ventricle, with severe myocardial degeneration. The kidneys showed only mild toxic nephrosis. Histologically, the brain showed evidence of increased intracranial tension of long standing which had developed on the basis of venous stasis.

We believe that in this case there are demonstrated clinically the conditions experimentally produced by Cushing and Raab, namely, elevation of the systemic blood pressure due to increase in intracranial tension. This case is not an isolated instance, as is shown by the accompanying table.

Comment.—Twenty-one of the patients indicated in the table were under 40 years of age; all showed increased intracranial tension with associated arterial hypertension. The autopsies were performed at the Philadelphia General Hospital during a period of two years. In no case was there histologic evidence of systemic arterial or renal disease. Any case was excluded from the series in which there was the slightest degree of arterial or renal disease.

This series of cases shows that the relationship between increased intracranial pressure and hypertension, which has often been observed clinically in cases of tumor of the brain or fracture of the skull, holds also in cases of more chronic increase in cerebral tension from various causes. The observations suggest that high blood pressure is a compensatory mechanism for lack of oxygen in the medullary centers.

DISCUSSION

DR. TEMPLE FAY: Dr. Scott has called attention to an interesting series of cases. There is no question that in a certain group of cases of benign hypertension with increase in the intracranial pressure or the volume of the cerebrospinal fluid there is associated arterial hypertension.

At a meeting of the Cushing Society in Rochester, Minn., in April 1936 I described a group of cases of this type in which a favorable response had been obtained with methods of dehydration and reduction of increased intracranial pressure and the volume of the cerebrospinal fluid. Cushing and others have shown that gradual increase in intracranial pressure is associated with a rise in blood pressure. This, in my opinion, appears to be a compensatory mechanism against "cerebral anoxia."

I wish to ask Dr. Scott if in the cases which he reported there was clinical evidence of increased intracranial pressure on spinal puncture and to what degree this increase was present.

Anoxemia of the nucleus of the vagus nerve has been mentioned as being responsible for the rise in blood pressure. Is it true that selective anoxemia of the vagus nerve has been established as the cause of this rise, and are the pathologic observations sufficiently convincing to establish this as under the regulation of the vagus nerve?

Local compression of the vagal nucleus or the area about the floor of the fourth ventricle is not sufficient to explain hypertension; I have observed patients with tumor in this area, with direct compression, who did not show hypertensive

phenomena. Hypertension may be a response to anoxemia, but I have not observed that section of the vagus nerve or injury to its nucleus is a cause of hypertension.

I wish to ask what correlation determinations of the spinal fluid pressure in this series proved to have with the pathologic changes that have been demonstrated.

DR. E. SPIEGEL: I wish to ask how the area of the vasomotor center in the reticulate substance appeared in these cases. The posterior inferior cerebellar artery supplies mainly the lateral part of the medulla oblongata, as shown in cases of Wallenberg's syndrome. The area of the nuclei of the vagus nerve has nothing to do with vasomotor control. The area of vasomotor control is below the central gray matter. I wish, therefore, to know how the reticulate formation was affected.

DR. GEORGE GAMMON: Dr. R. S. Griffith, Dr. W. A. Jeffers and Dr. M. A. Lindauer are studying a form of chronic hypertension in small laboratory animals which occurs after injection of particles of kaolin into the cisternal space. They find that they can readily induce sustained hypertension, and I believe that their explanation is: Increased intracranial pressure is secondary to blockage of lymphatic drainage.

DR. HELENA RIGGS: In answer to the first question of Dr. Fay about evidence of increased intracranial tension: I agree with Cushing that the actual pressure reading on the manometer is not a criterion for the degree of intracranial pressure, especially if the increase in pressure has been chronic and slowly progressive. There may be block at the foramen magnum with a low pressure reading, and yet at autopsy evidence of intense swelling of the brain may be observed. My associates and I employ the following criteria in the diagnosis of increase in intracranial pressure: (1) obliteration of convolutional markings in a brain which fits tightly within the skull; (2) molding of the inner table of the skull by the markings of the brain; (3) evidence of long-standing pressure on the hippocampi and the cerebellar tonsils, and (4) erosion of the clinoid processes and the dorsum sellae. Further substantiation of increased intracranial pressure, which is always due to cerebral circulatory insufficiency, is given by the microscopic evidence of cerebral anoxemia of the brain. This is particularly important in the areas around the third and fourth ventricles.

In answer to the second question: There is a characteristic microscopic picture of the brain in cases of increased intracranial tension. This is often obscured, however, by the primary pathologic changes.

In answer to Dr. Spiegel: The slide demonstrated showed evidence of degeneration of the myelin sheaths in the reticular substance of the medulla. There were also changes in the ganglion cells.

As to the blood supply of the dorsal nucleus of the vagus nerve. I cannot agree with Dr. Spiegel. There has been little study of the distribution of the arteries of the medulla. My colleagues and I have recently completed examination in about 400 cases and have observed that the blood supply varies more in this area than in any other part of the distribution of the circle of Willis. Frequently one posterior inferior cerebellar artery forms an anastomosis across the midline, so that the greater supply is from the vessel of one side, the other artery being rudimentary. In other cases, nine tenths of the blood supply to the entire brain stem is from one vertebral artery. I do not believe that Dr. Scott and I gave the impression that vasomotor disturbances are due to involvement of the dorsal nucleus of the vagus nerve. The dorsal longitudinal bundle of Schultze lies just above this nucleus and is thought to carry descending impulses from the hypothalamus. I think that this bundle was obviously degenerated in our sections. However, most workers agree that the exact localization of the areas controlling vasomotor or any autonomic function is still uncertain.

In our series there were 2 cases of mechanical compression of the medulla—in one by a slow growing astrocytoma in a child, and in the other, by chronic subluxation of the atlas. There were 4 cases of glioma of the hemisphere. Although our series is still small, we believe that not every glioma causes sufficient

intracranial tension to produce hypertension. In cases of tumor of the temporal lobe with encroachment on the hyopthalamus arterial hypertension was found. In all the rest of our series of 28 cases the increase in intracranial pressure was part of progressive circulatory insufficiency, which was magnified in the brain by the nature of the closed cavity of the skull.

DR. TEMPLE FAY: I still do not see that there has been presented any verification of pathologic changes to establish the existence of increased intracranial pressure. Is Dr. Riggs using this term from a clinical standpoint or as a pathologic deduction?

I think that the portion of the paper referring to increased intracranial pressure should be modified to indicate whether this term is used to denote actual increase in pressure as shown in the spinal manometer or secondary changes in the pathologic specimen that appear to be the result of pressure. Increased intracranial pressure means to me only one thing—increase in pressure above 8 or 10 mm. of mercury, which is normal—and one cannot speak of increased intracranial pressure unless by use of the manometer, with standardized technic, the pressure has been shown to be increased.

DR. HELENA RIGGS: If Dr. Fay is unwilling to grant my criteria of increased markings on the inner table of the skull and erosion of the dorsum sellae as evidences of increased intracranial pressure in the face of a normal reading on the spinal manometer, I can only refer him to Cushing's conclusions in the article entitled: "Some Experimental and Clinical Observations Concerning States of Increased Intracranial Tension," Mütter Lecture for 1901 (*Am. J. M. Sc.* **124**:375 [Sept.] 1902).

USE OF PROSTIGMIN AS A DIAGNOSTIC TEST OF MYASTHENIA GRAVIS. DR. GEORGE D. GAMMON and DR. HAROLD SCHEIE.

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DISCUSSION

DR. MATTHEW T. MOORE: Some cases of myasthenia gravis are difficult to distinguish from those of muscular dystrophy. The response to prostigmin will assist in differentiating the two conditions, the response in myasthenia gravis being prompt and pronounced while that in the dystrophies is slow and not marked, or may be lacking entirely. Again, meningovascular syphilis may show ptosis of the lids simulating the picture of myasthenia, and here prostigmin acts as a differential diagnostic agent. Films are shown to illustrate the use of prostigmin as an agent of diagnostic value in conditions thought to be muscular dystrophy or meningovascular syphilis but which proved to be myasthenia gravis, and in a case of neurosyphilis simulating myasthenia and one of an interpeduncular lesion producing complete paralysis of the third nerve, in which there was no response to the use of prostigmin.

DR. GEORGE D. GAMMON: I wish to point out that, while other persons have shown that various lesions of the peripheral and central nervous system do not respond to this drug, both Dr. Viets and I have found that various muscular diseases also fail to respond. As far as we can say, then, only myasthenia gravis is benefited by the use of this drug; should any other form of weakness improve, I think it will be time to reconsider the mechanism involved in such a condition.

MECHANISM OF THE GRAND MAL CONVULSION: PRELIMINARY REPORT. DR. K. M. CORRIN, Wernersville, Pa.

A clinical study of the major convulsion was carried out on a series of patients at the Wernersville State Hospital and experimental work was performed on a group of laboratory animals. Study of the major convulsion from the anatomic and the physiologic standpoint reveals much evidence to suggest, both clinically

and experimentally, that the convulsion is nature's safety-valve—a beneficial, physiologic mechanism to readjust disordered intracranial circulation and pressure. This pressure stimulation, producing the convulsion, is the result of blood entering the capillary bed of the brain faster than it can pass through, which causes sudden expansion outward of the brain tissue in all directions, forcing downward the sensitive brain stem into the constricting foramen magnum. Strong pressure stimulation at this site (medulla oblongata), producing the convulsion proper, results in the following series of systemic effects to relieve the dangerous intracranial pressure: (1) sudden, complete stopping of the heart and inflow of blood into the brain; (2) institution of the clonic phase, with its strong muscular activity, to stimulate the venopressor system, which is the great circulatory equalizer and stabilizer, and (3) production of somnolence and amnesia, which are in themselves beneficial in that they act as a sedative on the excitable nervous system, tending, with other factors, to quiet the neurocirculatory action.

DISCUSSION

DR. TEMPLE FAY: Dr. Corrin has presented an interesting review of the problem of convulsive seizures and has pointed out certain factors that may promote such a response. Herniation around the foramen magnum with compression of the medulla is not, however, a common occurrence. In the majority of epileptic subjects an encephalogram shows no such herniation; there are, in fact, in most instances large collections of fluid with actual diminution in the size of the structures of the posterior fossa. Furthermore, when herniation of the cerebellum occurs in association with tumor of the cerebellum or of the fourth ventricle, convulsions are clinically rare. Direct compression or involvement of the medulla by a tumor rarely, if ever, causes convulsive seizures. Stimulation in this area is incapable of producing a typical major convulsion.

I have produced convulsive movements in the human subject by stimulation of the cortex and of the cerebral mass at the level of the mesial wall of the thalamus, but never below this point. A typical convulsive seizure is not obtainable in the decerebrate type. A modified form of so-called spinal epilepsy may arise, but this is rather in the nature of irregular jerking movements similar to those of the reaction of defense. I am sure that direct pressure on the medulla alone cannot account for a typical convulsive seizure, although the medulla may mediate to some degree in the process. Selective anoxemia, in all probability, plays a large part in the convulsant mechanism, but the interrelationship of various levels and the pathways and factors concerned in the spread of the impulses are as yet unknown.

DR. ERNEST SPIEGEL: The theory of a rhombencephalic origin of convulsive disorders dates back to the last century. Convulsions may be produced by some toxins in decerebrate animals. The reticulate substance of the rhombencephalon may also be involved secondarily in convulsions of cortical origin. Several years ago I made experiments on this point. Median sections of the forebrain, including the corpus callosum and the anterior commissure, and of the diencephalon were produced. Apparently it was necessary for the stimulus originating in the motor area and producing general convulsions to descend to the rhombencephalon and then to ascend to the opposite cortex. These experiments, at the same time, emphasized the importance of the cortex in the genesis of clonic spasms. If I stimulated the cortex on the left side after injuring a part of the right cortex, tonic-clonic convulsions appeared in the right limbs, while the parts of the left limbs corresponding to the injured right cortex did not participate in the clonic component of the convulsions.

As to vasomotor reactions: Several years ago I showed that marked increase in the cortical plethysmogram occurs during convulsions. In making a record of the blood pressure and the volume of the brain, one must distinguish two factors: the direct effect of the vasomotor changes and the secondary effect of muscular contraction, since muscular contractions induce a rise in blood pressure. If one

wishes to study the effect of stimulation of the cortex on the vasomotor system, experiments on curarized animals are necessary.

DR. HELENA RIGGS: When Dr. Corrin first mentioned his observations on medullary compression my colleagues and I began to study the foramen magnum in relation to the medulla. This region was examined in all cases of epilepsy and in any case of epileptiform seizures. We have found that in 75 per cent of the cases in which clinical evidence of medullary involvement is given there is congenitally poor development of the posterior fossa, producing a funnel-like structure, so that the cerebellar tonsils are likely to herniate when pressure is increased. Furthermore, in these cases the posterior arch of the atlas protrudes anteriorly beyond the edge of the foramen magnum, with resulting constriction of the space between the odontoid process and the arch of the atlas. This means that the medulla is chronically compressed and that there is little room for expansion when edema occurs. Dr. Donaldson has discovered similar congenital defects in the foramen magnum of rats. The change occurs in strains which have been bred for generations in captivity. Thus, the wild Norwegian rat has a more normal foramen magnum than those of the Wistar strains, which have been bred in captivity for about seventy generations.

DR. K. M. CORRIN: There are two distinct types of intracranial pressure. I think that in the type under consideration pressure is produced rapidly, in a few seconds, and is more physiologic than pathologic in character—such as is seen in sudden straining or great emotion. If the cerebrospinal fluid is unable to leave the intracranial space quickly and allow the capillaries to dilate rapidly enough to accommodate the sudden increase in blood flow, there must be a sudden rise in intracranial pressure. In slowly produced intracranial pressure convulsions are rare. I have tried, after performing laminectomy, to place a ligature about the medulla so as to produce a gentle pressure stimulus at this site. The slightest touch, however, throws the animal into convulsive movements, with respiratory and cardiac arrest. The medulla is so sensitive to touch that this procedure has been uniformly unsuccessful. In one cat, after a series of convulsions lasting ten hours, with the animal dying in status, laminectomy in this area showed a white pseudomembrane over the medulla suggestive of prolonged irritation.

Dr. Fay spoke of cases of cerebellar lesion in which no convulsions occurred. The nervous system makes great accommodation for pressure in slowly produced pathologic states. I doubt whether slowly developing pressure of any type, acting alone, produces grand mal convulsions. The question of arrest of the heart with high blood pressure was raised. This cardiac arrest is striking when seen under the fluoroscope. Pressure is probably due chiefly to somatic muscular contraction, forcing venous blood back into the brain. Pressure from the action of the heart is out of the question at this stage.

The hypothesis of stimulation of the motor cells of the cortex is at present the general conception of the cause of convulsions. The complete cycle of the convulsion proper is from a few seconds to two or three minutes at the most. It is difficult to understand how a drug acting on cortical cells can stimulate them so rapidly. The most logical type of stimulus would seem to be sudden pressure at a point where motor, sensory, sympathetic and parasympathetic pathways are in close proximity.

CHRONIC ENCEPHALITIS: SYMPTOMATIC TREATMENT WITH BENZEDRINE SULFATE.

DR. ROBERT A. MATTHEWS.

This paper deals with the clinical results observed in 20 patients with chronic epidemic encephalitis and the parkinsonian syndrome who have been receiving benzedrine sulfate by mouth for from five to nine months. Seventy-five per cent of the patients have shown definite sustained improvement, which must be attributed to the drug alone since no change was made in the medical regimen which previously had been carried out. In another case some sustained improvement has been noted, but in view of an alteration in the previous medication, it is

questionable whether the change is due to benzedrine alone. One patient was better at first, but improvement has not been maintained. One patient has not been helped; 2 patients whose symptoms were aggravated subjectively by the drug refused to continue its use.

The improvement noted has not been the same in all cases. Oculogyric crises were controlled or diminished in frequency and severity in 5 of 6 patients. In 2 patients with myotonic closure of the eyelids the symptom was greatly benefited. Thirteen patients have manifested distinct improvement in mood; they have become more cheerful and state that they have more energy. There has been lessening of rigidity and tremor in a number of patients, but this has not been constant and is difficult to evaluate clinically. In 4 cases salivation has become less troublesome.

The blood pressure has been raised 10 mm. or more in 9 patients, has not varied more than 10 mm. in 10 patients and has been reduced more than 10 mm. in 1 patient. Initial low blood pressure was found in the majority of these patients, 11 having a systolic pressure below 100. The maximum rise in pressure in any case was 30 systolic and 20 diastolic. The patients whose blood pressure has been raised materially are in most instances those whose pressure was originally low.

The pulse rate was lowered more than 5 beats per minute in 8 patients, did not vary more than 5 points in 8 patients and was increased in 4 patients. Since the maximum effect of the drug, as manifested by changes in the blood pressure and pulse rate, is said to occur from ten minutes to one and one-half hours after administration and is continued for several hours, the recorded readings were made near the height of the reaction, since the patients were seen between 10:30 and 12 a. m. and the largest daily dose was directed to be taken at 8 a. m.

There was a gain in weight of 1 pound (0.5 Kg.) or more in 10 patients; the weight remained unchanged in 5 patients, and there was a loss of 1 pound or more in 5 patients. Loss in weight, with one exception, occurred in patients who were originally somewhat overweight. The results of the studies made so far have been encouraging and suggest several investigations. Although a large percentage of the patients have been benefited, the improvement can hardly be expected to be other than symptomatic, and it is questionable how long it will be maintained. Nevertheless, if these patients can be helped temporarily and given a more cheerful frame of mind, something has been accomplished, particularly in persons in whom the disease process has apparently become stationary. It is not possible at this time to evaluate to what extent the improvement has been based on psychogenic factors. An attempt will be made in the future to determine this by the use of a placebo in a group of patients used as controls. In addition, studies of the effect of the drug in this series of patients may help to throw light on its possible efficacy in other types of illness.

DISCUSSION

DR. A. GORDON: Was tremor diminished or increased?

DR. R. A. MATTHEWS: In no instance was tremor increased in patients in whom other drugs were continued. On the other hand, I could not measure any definite sustained improvement in this respect, although I think there was a little improvement in some cases.

DR. B. J. ALPERS: My experience with the use of benzedrine has been almost uniformly disappointing. I have noted no effect except subjective improvement in patients complaining of drowsiness. Even such small doses as 2 or 3 mg. twice a day produced gastro-intestinal symptoms, and in my hands it has been of no value in the treatment of encephalitis.

DR. R. A. MATTHEWS: I cannot explain why Dr. Alper's patients showed more side-effects than mine. The doses he gave were small. I do not think that doses of that size will be likely to produce any effect in cases of encephalitis. In one case I gave as high as 90 mg. a day for two and one-half months without disturbing sleep. The patient began to complain of insomnia, which required lowering the dose. The average dose was between 30 and 50 mg. daily. I have not observed any patient whose gastro-intestinal symptoms were severe enough to necessitate discontinuing use of the drug.

NEW YORK NEUROLOGICAL SOCIETY AND PHILADELPHIA NEUROLOGICAL SOCIETY

Joint Meeting, April 6, 1937

THOMAS K. DAVIS, M.D., *President of the New York Neurological Society, in the Chair*

DYSKINESIAS: PRESENTATION OF CASES FROM THE NEUROLOGICAL SERVICE OF THE MONTEFIORE HOSPITAL

PRESENTATION OF A CASE WITH MOVING-PICTURES. DR. S. PHILIP GOODHART, New York.

The first case is illustrative of a group of bizarre reactions in human behavior which are of particular interest to the neuropsychiatrist. It concerns the interplay of the cerebral cortex and sensorimotor and vegetative functions at structurally lower levels—the basal ganglia and the extrapyramidal system—in other words, the relation between the conscious and the subconscious, the organic and the psychogenic. Such reactions invite study as to the possible transition of a purely functional pattern to an organic pathologic state, that is, the transition of an original design and pattern as produced by cellular action to a fixed structural organization. I am reminded of the presentation by Dr. Tilney and me before the American Neurological Association several years ago of a series of moving-pictures, in which it was demonstrated that a patient who showed organic and psychogenic elements with bizarre dyskinetic movements ultimately presented the characteristic picture of dystonia musculorum deformans. The patient died recently, and microscopic study revealed characteristic pathologic changes.

There is a suggestive relationship between the motor pattern of hysteria and the extrapyramidal syndromes. The case to be described illustrates some points of differentiation. I believe there are both psychogenic and organic features, the first predominating. It is possible that the hysterical person may be born with an unstable extrapyramidal system, and loss of cortical control may bring it to the fore. In like manner, I wonder if in this case the exposure of a susceptible person to the baneful influence of metals might not have had a similar effect. It is not unlikely that in this case an organic pathologic condition may yet develop.

A married man aged 29 has one child, about 2 years of age. The family and the past personal history are essentially without significance. The mental and the physical development have been normal. For twelve years, at various periods, he worked in an atmosphere in which he may have been exposed to such metallic poisons as lead, arsenic, nickel and copper; he denies having had any direct contact with these metals. There is no evidence of preexisting encephalitis. He gives a vague history of daily vomiting for several months in 1932. The suspicion of pseudohypertrophic dystrophy was removed by taking for biopsy a specimen from the hypertrophied muscles of the left calf.

The relation of the appearance in 1935 of the early symptoms to intense emotional distress, anxiety and frustration is not clear. At this time he complained of pain, numbness and a tingling sensation in the toes and in the fingers; there is said to have been edema of the pendulous lower extremities and patchy cyanosis. A few months later, during a period of domestic infelicity attended by the emotional reactions mentioned, the present picture developed gradually. There were monotonous vocal intonation and postural changes of the body, bizarre in part and suggestive of a psychogenic origin, together with a syndrome indicative of pathologic changes in the basal ganglia: fixed facies, salivation, rigidity of the trunk and extremities, supranuclear facial weakness on the right and oiliness of the skin of the face. With hypnotic suggestion (by Dr. Leo Stone) the picture changed, and improvement was marked, with almost entire recession of the dyskinetic fea-

tures. This is shown in the film presented. When psychotherapy, including hypnotic suggestion, were omitted for a time, the dyskinetic picture reappeared with a state of emotional depression.

DYSKINESIA: PRESENTATION OF CASES. DR. I. S. WECHSLER, New York.

Dystonia musculorum deformans is a familial disease which occurs early in life and is marked by muscular contractions and variations in tonus, resulting in peculiar distortions. It was described by Ziehen and Oppenheim. It seems to me that dystonia is not a disease. Like chorea, it is a symptom which may occur on the basis of any number of pathologic processes. It may be part of various dyskinetic syndromes, or it may dominate the clinical picture. About fifteen years ago Dr. Samuel Brock and I (Dystonia Musculorum Deformans with Especial Reference to a Myostatic Form and the Occurrence of Decerebrate Rigidity Phenomena, ARCH. NEUROL. & PSYCHIAT. **8**:538 [Nov.] 1922) stated that we could split the syndrome of dystonia musculorum deformans into two types: a myokinetic and a myostatic form. Our reasoning was based on the observation of patients who passed from one phase to the other over periods of time. The patients more or less permanently assumed the posture which they showed momentarily between the phases of movement. Normally, in order to perform a given movement, one must "get set," i. e., one must assume a posture and then change from one posture to another. Indeed, movement may be defined as a series of postures. In myostatic dystonia the patient becomes frozen, as it were, in a given posture. The patient Dr. Goodhart has shown may possibly present one such phase; whether the explanation of psychogenesis is correct I do not know.

My first patient, a man aged 47, has been in the Montefiore Hospital about eighteen years. He tells of having had injuries, of operations and of injection of alcohol into one arm. All these stories must be discounted, or deductions must be made from his present condition. He showed dystonia in all muscles, not marked but universal. The movements have gradually ceased, and he has literally "frozen" into the posture he has maintained all these years. This is one of the cases which gave Dr. Brock and me a basis for the description of the myostatic variety of dystonia musculorum deformans. A recent encephalogram showed atrophy of the brain and cerebellum. The pathologic changes in dystonia are widespread; they include the cortex, the thalamus and other basal ganglia, the midbrain, the pons and the cerebellum.

The second patient, a man aged 30, was admitted to the Montefiore Hospital in 1924, at the age of 17. The disease began at the age of 9 years and developed after the fashion of classic dystonia. He has had various operations, in a vain effort to obtain relief; he still presents a fairly typical myokinetic form of dystonia.

The third patient, a youth aged 17, was admitted a year ago. There is a history of difficult labor. He began to walk at the proper time and to talk at the age of 15 months. He began to fall at the age of 18 months; since this time the dystonic picture has developed gradually. He, too, has had tenotomies.

The first patient I present shows the postural elements, though he displays also mild dyskinesias.

DISCUSSION

DR. BERNARD SACHS: Has this pattern been continuous?

DR. I. S. WECHSLER: Yes; almost continuous.

DR. BERNARD SACHS: Has it been so since the onset?

DR. I. S. WECHSLER: No; when I first saw him, he had more movement than he has now.

The second patient has been working in the hospital. At times his movements are much more violent than at others. He can slow down and assume a bizarre posture, which he is able to hold in order to carry out certain purposeful movements; hence, he is kept busy at the hospital. This condition began in the classic fashion in the lower extremities, then progressed from one limb to another, then to the body and finally to the neck.

In the third patient the illness began early in life, slightly contrary to the usual type of dystonia described by Ziehen and Oppenheim. The boy has learned what for him is the optimum posture, by which he can overcome some of the movements. He will lie face down on a wheel-chair made after his own construction. When he assumes that posture most of the movements cease. It is only when he begins to change position that the movements begin to come violently into play.

DR. BERNARD SACHS: What is he carrying in his hand?

DR. I. S. WECHSLER: A rubber ball; he thinks he can walk better if he has it. His intelligence quotient is 99. He finished public school, despite the movements, and even attended high school for a time.

DR. BERNARD SACHS: What was the beginning in this case?

DR. I. S. WECHSLER: It dates back to early childhood. There is a history of eight hours of difficult labor and of cyanosis at birth. The trouble began gradually at the age of 18 months, after he had learned to walk well.

DR. BERNARD SACHS: Does he fall now?

DR. I. S. WECHSLER: Rarely; he can protect himself fairly well.

The point I wish to make is that there are two forms of dystonia—a myostatic type, in which posture predominates, and a myokinetic type, in which dyskinesia prevails. The postural type represents a temporary or a permanent stage of transition. I have seen patients who for a time showed the myostatic variety and then passed into the myokinetic stage. The illness may begin as a postural form. I have seen the condition in some cases go through the various forms and end with a parkinsonian syndrome; in those instances the disease has occurred on an inflammatory basis. In the main, I assume that the process is degenerative.

I wish also to point out that all the movements have a pattern; they seem to be, as Wilson indicated, subjectively purposeful and objectively purposeless. The patient starts as though he were about to make a purposeful movement, but he never "gets there." The whole picture resembles chorea, except that there is a much larger movement, which involves axial as well as appendicular muscles. In chorea there is the same type of variation in tonus. The two phases of dystonia which I demonstrated are merely different aspects of one disease.

UNUSUAL CASE OF MYOCLONIC EPILEPSY. DR. MOSES KESCHNER, New York.

A man aged 46 was admitted to the Montefiore Hospitla with the chief complaint of violent jerkings of the body. He was born in Russia and has been in the United States for twenty-five years. He has not worked for the past ten years; prior to that he was a clothing operator. He was never exposed to intoxication with heavy metals and rarely drank alcoholic beverages. He is married and is the father of a healthy son. His wife has had no miscarriages.

The patient had measles and bilateral otitis media in childhood. At the age of 17 he had a penile lesion which was neither associated with nor followed by the usual manifestations of syphilis. At the age of 27 he had an attack of influenza, which ran an uneventful course. There have been no other illnesses.

The patient's father died at the age of 44, of apoplexy. His mother is living and well. There is no consanguinity. One of his mother's sisters at the age of 50 had a condition resembling that of the patient. A second cousin on the mother's side suffers from convulsions. A third cousin of the mother had a condition similar to that of the patient at the age of 22 and died at 43. A brother died at the age of 26 in an institution for the feebleminded, where he is said to have had a disease resembling multiple sclerosis with myoclonus and ataxia; he had no convulsions; his mental age at 26 was 4 years and 4 months. A daughter of the patient's brother had a convulsion during a febrile disease in childhood.

At the age of 30 the patient began to have spasmodic jerkings, of lightning-like rapidity, in the upper extremities and the muscles of the neck; these persisted for about three years, when they appeared also in the trunk and lower extremities,

so that he sometimes fell and injured himself; on one occasion he fell and fractured the left zygoma; on other occasions he sustained various injuries to the limbs. The jerkings appeared most of the time spontaneously; at other times they were initiated by emotional upsets, sudden noises or exposure of the eyes to light. The frequency of occurrence of the jerkings varied; he had good days, on which the attacks occurred only a few times during the day, and bad days, during which the jerkings followed each other in rapid succession with short free intervals. There were no days during which he was free from attacks. During some attacks the eyelids closed and trembled. During others the eyes remained open; the head was turned to the right, and the right side of the body became rigid and also turned to the right; during still other attacks there occurred facial grimacing associated with grunting respiration. On several occasions, after cessation of these attacks the face assumed a blank expression and the patient became cyanotic, but he is said to have retained consciousness.

In January 1932, while in bed, the patient had a general convulsion lasting about ten minutes; he was unconscious for a half-hour. During the next four or five hours he was very weak but was free from jerkings. After this, however, the jerkings increased in frequency and severity. Three months later he was admitted to a hospital, where encephalography disclosed marked atrophy of the cerebral cortex, especially in the frontal region.

In spite of vigorous treatment with sedatives, the condition became progressively worse. During the past few years there have appeared disturbances in speech and incoordination of all four extremities and an abnormal gait.

Examination.—The essential findings on admission to the hospital were: (1) myoclonic movements in the muscles of the face, neck, trunk and all four extremities; (2) bilateral deafness due to disease of the middle ear; (3) inconstant nystagmus in all directions; (4) slight weakness of the left external rectus muscle; (5) moderate sclerosis of the retinal vessels; (6) slight facial weakness on the right side, elicited only on mimetic innervation; (7) choreiform movements of the tongue; (8) broad-based, ataxic gait with dyssynergia of all four extremities; (9) rigidity of the left lower limb with a tendency to the cogwheel phenomenon; (10) a suggestion of a rebound phenomenon in both upper extremities, and (11) cerebellar speech. Otherwise, neurologic examination revealed nothing abnormal. All laboratory findings, including those of the spinal fluid, were normal.

Mental State.—The patient is said always to have been peculiar. He was unusually irritable, moody and boastful and had a tendency to exaggerate situations in which he was involved. During the past ten years his superiority complex has become more intensified and his lying more marked. On several occasions he had delusions of marital infidelity and of persecution. He is said to have had visual and auditory hallucinations. At times he is euphoric and facetious. He is evasive in answers and given to circumlocution. He is slow in thought, speech and action. His memory is poor for recent as well as for past events; both retention and recall are affected. There is no question that there is progressive mental deterioration.

Comment.—The patient is suffering from a progressive degenerative disease of the central nervous system. The disease is apparently diffuse, involving the cerebral hemispheres, basal ganglia and cerebellum. In view of the family history, the condition is probably a heredofamilial form of a primary degenerative disease, with myoclonic epilepsy as the most pronounced clinical feature. Phenomenologically, it is difficult to classify the condition and to include it among the usually recognized heredofamilial symptom complexes. Although one has a fairly good conception of the nature and site of the lesions responsible for the patient's mental symptoms, incoordination, speech and slowness in initiating voluntary movements, there is no adequate explanation for the cardinal manifestations of the disease, namely, the myoclonus and epilepsy. Lesions in almost every part of the central nervous system, even in the muscles, have been held responsible for myoclonia. With the clinical evidences in this case of diffuse involvement of the central

nervous system, it would be futile to attempt, at least on clinical grounds alone, to express an opinion as to the pathophysiologic picture of the most striking symptom which the patient presents, i. e., the myoclonus.

DISCUSSION

DR. SAMUEL B. HADDEN, Philadelphia: This is a magnificent group of cases; I have little to add to what has already been said by Drs. Goodhart, Wechsler and Keschner. I think that Dr. Wechsler's point that dystonia is a symptom rather than a disease is well taken and that his emphasis on the fact that dystonia may change and assume a static state is also of importance. Differential diagnosis is frequently discussed and may lead to heated argument as to whether a particular case is one of dystonia musculorum deformans, or of a similar extrapyramidal disorder; such metaphysical discussions are not helpful to the problem. The differential diagnosis is many times difficult to make, because one man sees the condition at an entirely different stage from another. The field of the dyskinesias is one of the most difficult in neurology, and the clinical classification is about as difficult because of the confusion of ideas as to the function of the various basal ganglia and cerebellar centers and the cerebellar relations to coordination. I believe that pathologic study has not helped in determining the function of the various basal ganglia and cerebellar centers; I think also that experimental work on animals will do little, for, as Magnus pointed out, there is little relation between the basal ganglia of experimental animals and those of man. Magnus was unable to cause any disturbance in an animal's motility by a lesion of the extrapyramidal pathway above the red nucleus.

DR. E. A. SPIEGEL, Philadelphia: I was much interested in these presentations, not only from the clinical but from the pathophysiologic point of view. In the last decade one has made the differentiation of static and kinetic innervation; this differentiation of two types of central action has great value. One must bear in mind, however, that these two types of innervation interplay in normal life—the postural innervation depending on the kinetic and vice versa. Kinetic innervation always acts on a certain postural background; whenever a movement is innervated, the outcome depends on the posture. On the other hand, each kinetic innervation changes the postural innervation. In other words, although the differentiation between kinesia and posture is justified, the two mechanisms act through similar and closely interrelated centers. This is shown in these pathologic conditions, particularly in those described by Dr. Wechsler, in which in the same case there was at one time more postural and at another more kinetic disturbances; the picture may again be reversed to the postural type. One must bear in mind that changes in the functional state of the nerve cells in the same pathologic state may give rise to different clinical pictures. The same lesions in the basal ganglia might produce athetosis in a child and chorea in an elderly person; so age plays a rôle. The action of toxins and the metabolism of cells may also play a part in changing the reaction, as indicated by experiments of Magnus. These clinical observations of Dr. Wechsler show well that the two types of innervation are closely related and that both may be shown in the same case.

In seeing these patients with hyperkinesia the question arises: What can one do for them besides making a diagnosis? One method, perhaps, is to destroy the centrifugal pathways of the extrapyramidal system. Putnam tried to sever the reticulospinal and vestibulospinal tracts in the spinal cord. Unfortunately, it is difficult to cut all these tracts in the spinal cord because they are arranged in a diffuse area; there is, however, perhaps another way of counteracting these hyperkinetic states, particularly in cases in which the lesion is in the pallidum. If it is true that the pallidum is the seat of the involuntary mechanisms, one can interfere with this state not only by severing the centrifugal pathways but possibly by diminishing the excitatory impulses acting on the pallidum. From where does this excitation come? Partly from the thalamus directly and partly by way of the frontopallidal and frontothalamopallidal tracts. The question arises whether it would be possible

to diminish the action on the pallidum which takes origin in the frontal lobe by operative procedures in the prefrontal area—I mean, not only by mechanical transection of the frontofugal fibers but by bilateral laminar thermocoagulation of this region.

DR. I. S. WECHSLER: The suggestion of Dr. Spiegel has been anticipated by Dr. Ira Cohen, who operated on a patient at the Montefiore Hospital. Unfortunately, not enough cortex was excised; it is not known whether the result might have been successful had more been removed. The operation was done on one side only. I did not wish to take time to discuss the relation of posture to tonus. The two are intimately related. It is reasonable to say that if one could affect tonus one might influence the dystonia. There are many points in the neuraxis which affect tonus: the neuromuscular junctions, the sensory roots, the posterior columns, the vestibular mechanism, the basal ganglia, the pyramidal tracts and, surely, the frontocerebellar pathways. Dr. Spiegel's suggestion, therefore, has theoretical validity. It touches one aspect of the problem.

A CLINICAL STUDY OF HERNIATION OF THE NUCLEUS PULPOSUS. DR. BYRON STOOKEY, New York.

In an attempt to correlate the clinical symptoms of protrusion of the disks it is necessary to distinguish between lesions of two regions of the vertebral column —cervical and thoracic protrusions, causing symptoms of disturbance of the spinal cord and roots, and lumbar protrusion, which involves not the spinal cord but the roots of the cauda equina.

Since I have nothing special to add to the clinical study of protrusion of the disks involving the spinal cord and nerve roots made in 1927, this report is limited to herniation of the disks in the lumbar region. No one has had the extensive experience of Dr. Mixter and his co-workers in Boston in their study of herniation of the disks in this region. The present series concerns 9 cases of herniation in which the diagnosis was verified at operation. In 5 cases the protrusion was between the fourth and the fifth lumbar vertebra, and in 3, between the fifth lumbar and the first sacral vertebra, or between the third and the fourth lumbar vertebra. One patient had associated compression due to thickening of the fifth lumbar vertebra. The average age of the patients was 37—the youngest being 23 and the oldest 57. Three patients were women and 6 men.

Pain was the presenting symptom in all 9 patients and was referred to the lower part of the back and down either the dorsal surface of the thigh and leg to the ankle or the anterior region of the thigh. Sensory changes were present in 5 cases, though they were vague and mostly subjective. Motor changes were the most constant findings; they may easily be overlooked. The most constant of these was slight atrophy—in the quadriceps muscle, the small muscles of the foot or the gluteal muscles. Occasionally, atrophy was noted in all muscles. Absence of the achilles jerk was the most constant change in the reflexes. Loss of lumbar lordosis and sciatic scoliosis were the most constant postural alterations.

Manometric examination of the spinal fluid showed block only in the patient who had associated compression of the cauda due to enlargement of the vertebral arches. The total protein content, in all cases except this, was only slightly elevated, the highest being 102 mg. per hundred cubic centimeters.

The final diagnosis rested on injection of 5 cc. of iodized poppy-seed oil. While this has been done apparently without unfavorable results, as yet, I have been reluctant to accept this method as the best diagnostic procedure. Accordingly, Dr. Scarff and Dr. Dyke and I have made a series of injections of air in the lumbar region, in order to visualize the lumbosacral subarachnoid space and, thus, to avoid the introduction of a foreign substance. Our results have been encouraging; I have shown today a slide indicating the presence of an obstructive lesion which was demonstrated by air, confirmed by injection of iodized poppy-seed oil and proved by operation.

Further studies are in progress and will soon be reported.

DISCUSSION

DR. FRANCIS C. GRANT, Philadelphia: Dr. Stookey's thorough presentation of this clinical picture does not leave me much to say, but three things are worth emphasizing. I have seen 3 patients in this series, of whom 1 had herniation in the cervical region and 2 in the lumbar region. The condition in all cases followed trauma. A cook with protrusion of an intervertebral disk in the cervical region had, on lifting a large pan of spinach from the floor into the sink, flipped his neck back and had then experienced pain; eventually there developed partial block, and operation was performed. In the other 2 cases the herniation was in the lumbar region. A German housewife was carrying two pails of milk on a yoke across her shoulders, when she slipped and sat down heavily on her buttocks. She complained of sciatic pain in the right leg during the next two years. She had atrophy of the right leg with loss of reflexes and some sensory lesions; at operation a lesion of the type described by Dr. Stookey was removed. The third case was similar; after trauma there was pain, and a diagnosis of sciatica was made, with the eventual discovery of a protrusion of the disk and its operative removal.

I am of the opinion that many more of these protrusions are overlooked than are operated on successfully. When one finds a history of pain following trauma, particularly, and subsequent sciatica, with the type of lordosis and scoliosis that Dr. Stookey has outlined, one should suspect that a lesion of this type is present. From my brief experience and the perusal of papers by Mixter and others, it would seem that one should pay particular attention to three points in reaching the diagnosis. One is the increase in protein following lumbar puncture. Manometric tests are notoriously unreliable. One rarely finds complete block, probably because the needle is introduced above the level of the lesion; even if one introduces the needle below this level, the lesion is often so small that, at most, only partial block occurs. Second, studies on protein are important. In one of our cases, it is true, there were complete block and a high protein content, but in the other 2 cases the protein content was 69 and 74 mg., which is not particularly high. Third, injection of 5 cc. of iodized poppy-seed oil is necessary to bring out the defects. Smaller amounts are not successful, because the lower part of the sacral canal is not filled. It is important to take the roentgen films with the patient in the prone position, since the tumor is anterior and one wants the oil to spread by gravity through the anterior portions of the canal; when the patient is in the prone position the canal is filled, and roentgenography reveals the deformity satisfactorily.

When one operates, it is sometimes difficult to locate the lesion; I imagine that in the past my colleagues and I, before we knew the nature of this condition, must have operated in some cases of this condition, thinking that the lesion was a tumor and that the exploration was regarded as without result because we did not know where to look for the trouble.

In the 3 cases in which I performed operation, the results were successful, with relief of pain, in the 2 instances in which the herniation was in the lumbar region; in the third case no functional recovery was obtained.

DR. TEMPLE FAY, Philadelphia: Only a few minor points can be touched on after Dr. Stookey's able presentation of this subject. Schachtschneider (*Fortschr. a. d. Geb. d. Röntgenstrahlen* **54**:107, 1936) reported 3 cases in which narrowing of the spinal canal was due to prolapse of the tissue of the internal part of the disk between the posterior longitudinal segment and the dura. His analysis may throw light on the neurologic side of this problem. So far, the diagnosis and localization depend to a large extent on mechanical means, such as the injection of iodized oil and air. The symptoms at times are not clearcut or localized discretely to the level of the lesion, and the signs may be referable to a level several segments higher. In 2 of the cases reported by Schachtschneider this was true. In 1 case in which there was a lesion at the level of the fifth lumbar vertebra, which lies well below the caudal end of the cord, a Babinski reflex was obtained. There were loss of the deep tendon reflexes and sacral anesthesia. One would not expect a Babinski reflex below the termination of the cord. Schachtschneider

called attention to the fact that some of these manifestations, pointing to involvement of parts higher than the actual lesion, were due to venous stasis produced by narrowing and obstruction of the canal, causing interference in the circulation about the portion of the cord above the level of the compression.

I am sure that stasis of the veins which surround the dura plays a large rôle in determining the symptomatic level of the lesion, which may be one, two or three segments higher than the actual localization by iodized poppy-seed oil or air would indicate.

From the neurologic standpoint the signs of root involvement are important as indicating the level of the lesion, but certain symptoms, such as hyperalgesia, perverted deep and superficial reflex responses, burning and pain, may be at a higher level, confusing the picture, and must be accounted for. They are not explained by the direct influence of a lesion in the lower lumbar area.

Dr. Stookey brought up the point of the use of iodized poppy-seed oil. I am personally adverse to the use of this oil. I do not like it for two reasons: First, after its injection it is difficult to reclaim, and, second, I do not think it is "sporting" from the standpoint of the neurologist and the art of neurology. If one hunts with a "pump" gun, one can hit almost anything; the art of neurology still lies in the attempt to make a diagnosis without mechanical means! Dr. Spiller taught that to those of us who were associated with him, and in Philadelphia we have tried to foster the diagnostic art. To obviate the need for the use of iodized oil, we have paid more attention to minute clinical phenomena and sensory determinations. Dr. Chamberlain and Dr. Scott, for more than a year, have given excellent visualization of the spinal cord by means of injections of air, which Dr. Stookey also uses, so that by means of a "myelogram" or "spinogram" one can visualize obstruction in the canal; this procedure does not require the employment of iodized oil. To prove the relative values of the two methods, we have combined the use of air with that of iodized poppy-seed oil. In instances in which partial or complete obstruction occurs, it can be shown that the column of air has stopped at a point where the obstruction exists.

I have selected 3 cases of prolapse of the nucleus pulposus from my series illustrating lesions at various levels—1 of a lesion at the tenth dorsal vertebra; 1, at the second lumbar vertebra, and 1, at the fifth lumbar vertebra.

In the first case, that of a woman aged 38, slight calcification may be seen at the level of the tenth dorsal vertebra. We thought that this was an enchondroma, because of the firm, hard shell observed at operation. The center of the tumor was soft and proved to be a chondroma. The pathologic material was similar to tissue of the nucleus pulposus; the capsule, however, had become eburnated. In this case, iodized oil was used and contrasted with the air. In the films the characteristic defect described by Dr. Stookey can be seen.

The second case, that of a man aged 36, is interesting because the patient is an achondroplastic dwarf. This is the only case I have seen in which there is direct evidence of trauma that can be regarded as the cause of the lesion. The patient was a circus dwarf, part of whose act was to fall into a net; on one occasion the net was not there and he fell on his back. There were no symptoms for several months, and mention of the incident was elicited only by careful questioning. In the roentgen film, however, there was observed crushing of the first lumbar body, giving a cuneiform distortion to the vertebrae. Dr. Chamberlain called attention to the fact not only that there is obstruction to the column of air (we have found that only from 3 to 5 cc. of air is necessary to produce excellent films) but that the canal itself is narrowed, probably as a result of the achondroplastic dwarfism. Prolapse of the nucleus pulposus into this small canal probably accounts for the finding of complete block in the Queckenstedt test, with Froin's syndrome. The position of the lesion between the second and the third lumbar vertebra, just under the tip of the sacral portion of the cord, was such that paralysis and loss of sensation were profound in the sacral distribution; however, there were no bladder disturbances. Definite root pains occurred in the first lumbar dermatome, with vasomotor disturbance and hyperalgesia.

In the third case, that of a woman aged 49, roentgenograms were made with the sacral portion of the canal elevated, i. e., with the buttocks up. The column of air shows the typical deformity (not demonstrated with iodized poppy-seed oil in the anteroposterior view, except for a slight indentation); in the lateral view a definite defect is apparent.

Finally, I wish to emphasize a point regarding operation. In this condition there is not alone a defect in the articulations between the vertebral bodies; the patient should have a firm posterior fixation, like the Hibbs fusion, so that a firm band of tissue will maintain a check-rein influence on overflexion.

I call attention to the technic we employ. An incision is made through the skin, and then with a sharp osteotome the tips of the spinous processes are cut away with the wall of the process, without disturbing the attachment of the muscle to the periosteum. This takes much more time than other methods of stripping away the muscles. Little bleeding occurs, and an excellent lateral approach to the cord is obtained in cutting the pedicle with disarticulation of the facet. In attempting to reach the anterior surface of the cord, wide lateralization of the approach is important, so as to avoid trauma in displacing the cord during a transdural attack on a lesion in the midline. This type of laminectomy affords an excellent approach to the lesion and a firm, strong back support when the periosteal layers and muscles are sutured together. The tip of each spinous process is brought to the fellow tip on the opposite side and strongly sutured with silk. Fusion at the midline occurs free from mobility, owing to the former laminal articulating facets. The patient is not required to wear a cast or brace, and after this type of laminectomy, instead of the depression in the back, which was noticeable formerly when reconstructive fusion was not made, there is almost normal alinement. At the end of three or four months there is a firm line of calcified periosteal tissues, which maintains the safety and integrity of the spinal canal.

DR. BYRON STOOKEY: I am grateful to Dr. Grant and Dr. Fay for their discussion. I am especially interested in Dr. Grant's comment on trauma as an etiologic factor and can say only that in 4 of my cases it was not possible to establish a history of trauma. When such a history is present, herniation of the nucleus must be considered.

There is particular interest in Dr. Fay's report of herniation of the disk at the fifth lumbar level in association with a Babinski sign, presumably due to this lesion.

In discussing ventral chondroma, I drew attention in 1927 to the fact that in the cervical region compression of the spinothalamic tract is two or three segments higher than the sensory level, owing to the oblique crossing of the spinothalamic fibers. Thus, if the spinothalamic tract is compressed at the fourth cervical segment, there will be a sensory level for pain and temperature corresponding to the sixth or seventh cervical segment. No such mechanism exists in the lumbar sac, in the region of the cauda equina.

Injection of air into the lumbar region has usually been made to demonstrate tumor of the spinal cord. In cases of this type block must be complete, and the tumor must act as a cork to obstruct the passage of the air. By tilting the patient's buttocks upward, I have recently used from 20 to 30 cc. of gas to outline the whole of the lumbosacral sac; by this method one is able to outline an impingement on the dura, such as a herniation of the nucleus pulposus.

As to the operation in the cervical region to which Dr. Fay referred: It is my opinion that in these cases approach should be made by hemilaminectomy, as advocated by Alfred Taylor in 1910. That is one of the most satisfactory methods of exploration of the cord when a ventral lesion is suspected, for it permits easy access to the ventral surface. I am sure that Dr. Fay would not think of exposing the lumbar region, as he showed in his picture, by taking off the articular facets. What he has shown in his lantern-slides must, I am sure, be intended for the thoracic, not the lumbar, region. In the lumbar region I should hesitate to do anything other than posterior laminectomy, avoiding carefully the articular facets. In the lumbar region, in particular, the facets are an essential part of the stability

of the vertebral column; if they are removed simultaneously with the spinous process and the laminae, the stability of the lumbar portion of the spine will be materially weakened. Hence, I am careful to preserve the articular facets.

I am delighted to hear that Dr. Fay exposes the spines and laminae by subperiosteal resection. I have done this for many years, and I agree that it is to be preferred, not so much because it makes for a stronger back but because there is less bleeding. It is, however, difficult to obtain complete subperiosteal resection. I do not apply plaster after laminectomy, and I am glad to hear that Dr. Fay does not.

RESULTS OF ROENTGEN TREATMENT OF TUMOR OF THE PITUITARY GLAND: REPORT ON 81 PATIENTS, 48 OF WHOM WERE TREATED EXCLUSIVELY BY IRRADIATION. DR. CLARENCE C. HARE and DR. CORNELIUS G. DYKE (by invitation), New York.

This paper presents the results of roentgen ray treatment in 81 cases of adenoma of the pituitary gland at the Neurological Institute of New York during the years 1929 to 1937. Twenty of these cases were reported in 1933 (Roentgen Therapy of Pituitary Tumors, *Arch. Ophth.* **10**:202 [Aug.] 1933) and are included in this study, with observations up to the present. Forty-eight of the patients had roentgen ray therapy only. Fifteen additional patients received this therapy for one month, but their condition became progressively worse or failed to improve and operation was performed. These 15 cases have been added to the 48 in which treatment was by irradiation only, since fairly adequate therapy had been given prior to operation. Thus, a group of 63 patients have been treated prior to any operative procedure. Eighteen other patients had roentgen therapy after operation; the results in that group are omitted from the present discussion. Only cases in which observation was made for one or more years after the institution of roentgen therapy have been included in the series. In all cases the diagnosis of adenoma of the pituitary was established clinically. Cases in which the diagnosis was doubtful were rejected.

In this presentation we are interested particularly in reporting the effect of radiation on vision, i. e., visual acuity and the visual fields, which is of most importance in this condition. In the group of 63 patients treated with roentgen radiation only, 25 had a chromophilic and 38 a chromophobic adenoma. Of 25 patients with chromophilic adenoma 8 showed marked improvement in vision and 2 slight improvement, and the condition of 9 remained unchanged. Thus, in 19 (76 per cent) of the 25 patients vision either improved or remained stationary.

Of the 38 patients with chromophobic adenoma 8 showed marked improvement and 2 slight improvement, and the condition of 10 remained unchanged. Thus, in 20 (52.6 per cent) of the 38 patients vision either improved or remained stationary.

When one considers the group of 63 patients collectively, 16 (25.3 per cent) showed marked improvement and 4 (6.3 per cent) slight or moderate improvement; the condition of 19 (30.1 per cent) remained unchanged, and that of 24 (38.3 per cent) became worse. Thus, the vision of 61.7 per cent of the patients treated by irradiation only either improved or remained stationary for one year or more.

What was the period during which vision was markedly improved? It extended from one and one-half to seven and one-sixth years. One patient maintained his improvement for seven and one-sixth years, 1 for six and one-half years, 1 for five and three-fourths years, 1 for four and one-half years, 2 for four years and 3 for three and one-half years, and the average period for the rest was two years.

In summary, observations on this group of patients lead us to conclude that irradiation is a valuable form of treatment of pituitary adenoma, regardless of the histologic type. It is necessary, however, that the visual fields and visual acuity be measured frequently.

DISCUSSION

DR. ROBERT A. GROFF, Philadelphia: I wish to compliment Dr. Dyke and Dr. Hare on the excellent presentation of this subject. I am particularly interested in this phase of treatment for pituitary adenoma, for I have gathered a few cases in which roentgen ray treatment has been the only form of therapy. In the cases which I have observed in the clinics the clinical diagnosis of chromophobic adenoma was made.

From the statistics which have been presented it seems that in the group of patients with chromophobic adenoma if one combines the percentage of those whose vision was unchanged and the percentage of those in whom the condition became worse, one obtains a figure of 60 per cent. In other words, in about 40 per cent of the patients there was definite improvement from roentgen therapy. If one combines similar percentages for the group of patients with chromophilic adenoma, one finds that vision in 74 per cent of the patients was either unchanged or became worse; in the few patients whom I have been able to follow the results have been more or less in keeping with these figures. Roentgen ray therapy, therefore, has proved effective in 25 per cent of the patients with chromophilic adenoma and in 40 per cent of those with chromophobic adenoma. These figures are impressive in that they show, first, the effectiveness of roentgen ray therapy and, second, the limitations of its effectiveness.

The important factor here is to establish a criterion for the use of surgical treatment and for the employment of roentgen ray therapy alone. It is only by studies such as have been made by Dr. Hare and Dr. Dyke that one will be able to come to a definite conclusion in regard to this problem. It has been my practice in cases in which there were definite cuts in the visual fields, diminution in visual acuity with primary atrophy of the optic nerve and increase in the size of the sella turcica to advise that surgical treatment be employed first. The primary necessity is decompression of the optic nerves and optic chiasm, and one should not wait for the time required to reduce the size of the adenoma by roentgen treatment. I have used these findings as the indication for immediate surgical treatment. On the other hand, in cases in which I have used roentgen therapy alone I have considered a moderate cut in the visual fields, possibly normal or slightly diminished visual acuity, more or less normal eyegrounds and some enlargement of the sella turcica as the findings which do not demand immediate surgical intervention.

With the evidence presented by Dr. Hare and Dr. Dyke the value of roentgen ray therapy has been demonstrated. The establishment of indications and contraindications for its use, such as I have given, is highly necessary if the patient is to receive suitable treatment at the proper time. Certainly, immediate surgical decompression of the optic nerves is indicated when visual acuity is failing rapidly and the optic disks show progressive atrophy.

DR. KARL KORNBLUM, Philadelphia: I find that the experience in the treatment of tumor of the pituitary gland reported by Dr. Dyke and Dr. Hare is similar to that which my colleagues and I have had in Philadelphia. There is no doubt that close cooperation between the various departments interested in the management of patients with pituitary tumor is the keynote to success, and it is obvious that such cooperation exists in the Neurological Institute. At the neurologic conferences conducted weekly at the Graduate Hospital of the University of Pennsylvania, in Philadelphia, under the able direction of Dr. Joseph C. Yaskin, patients with pituitary tumor are presented, and the cases are discussed from every possible angle. Thus, we have the opportunity of hearing the opinion of the ophthalmologist, the endocrinologist, the roentgenologist, the neurologist, the neurosurgeon and the neuropathologist. From these accumulated data an accurate summation of the case is obtained, and it becomes possible to determine the form of therapy for use in any particular case.

Dr. Groff has outlined the criteria we use for the application of roentgen rays. As a roentgenologist, and in spite of enthusiastic reports, I attempt to maintain a conservative attitude as regards the value of roentgen rays in the treatment of

pituitary tumor. It must be admitted that a tumor of the brain is not among the neoplasms which are sensitive to roentgen rays; while some tumors of the brain are more sensitive than others, a tumor of the pituitary gland is not particularly susceptible to roentgen rays; so a careful selection of cases must be made, such as I am sure was made in the series which Dr. Hare has reported.

The rôle of postoperative irradiation in the treatment of pituitary tumor is difficult to evaluate, for one never knows how well the patient might have done if he had not received radiation. In the case of the patient who receives nothing but roentgen ray therapy, however, there can be little doubt as to whether the treatment has or has not been beneficial. Those who have had the opportunity to follow these patients have seen some striking results.

Dr. Hare and Dr. Dyke have stressed the importance of visual acuity, but other symptoms and signs, while not as important, should nevertheless be, and I am sure were, considered in the cases reported. Headache is markedly improved in many patients with this tumor, and the weakness of which many of them complain is greatly ameliorated. In acromegaly the pudginess of the soft tissues is greatly reduced, and the visual acuity is improved. Nevertheless, in spite of the definite improvement of subjective symptoms, one can see progression in the size of the tumor by frequent roentgen observation of the sella turcica and by watching the visual acuity and the visual fields.

The technic that Dr. Dyke has outlined is somewhat different from ours, but essentially it works out to the same end. We have used somewhat larger total doses than he has employed in his cases. As a rule, we use the two lateral portals, with an additional third portal through the vertex, and at times we have employed as many as five portals directed toward the sella turcica. The treatment given through each portal has varied from 2,500 to 5,000 roentgen units. The patient with a tumor of the brain is fortunate in the respect that the head is highly tolerant to roentgen therapy. We seldom encounter any serious local or systemic reactions; giving as much as 5,000 roentgen units through the scalp need not produce any undue reaction, while this amount of treatment could not be given with safety through any portion of the skin of the chest or abdomen. Furthermore, patients receiving radiation to the head show little systemic reaction in the way of radiation sickness. I do not remember any patient for whom I have had to discontinue treatment because of roentgen sickness.

During the past few years we have been particularly interested in studying the effects of irradiation on the blood. In some patients there is a definite, though slight, tendency to anemia, while in most patients there is definite reduction in the number of leukocytes. These changes in the blood are seldom encountered in patients receiving radiation over the head; so the patient with a pituitary tumor is an ideal subject for roentgen therapy.

Dr. William Edward Chamberlain, Philadelphia: In any condition in which roentgen ray therapy gives favorable results in from 25 to 35 per cent of cases one is inclined, at least roentgenologists are, to maintain a pessimistic attitude; in other words, the cases in which there is failure, or lack of success, outnumber those in which there is a favorable response. One can find many other conditions in which the results are more unfavorable, or less favorable, than in pituitary adenoma, and still I think that the roentgenologist should maintain an unenthusiastic attitude toward the irradiation of a pituitary adenoma, for enthusiasm on his part may result in depriving some patient of a better form of therapy. It is well enough for the neurosurgeon to become enthusiastic about irradiation of pituitary adenoma, and this has been a satisfaction to those in this audience who are roentgenologists, but I maintain that the roentgenologist who permits himself to become enthusiastic on this subject is likely to run into certain pitfalls. First, he is likely to receive patients from those who are not so well equipped for diagnosis as are the speakers today, and he finds himself treating patients with conditions diagnosed as pituitary adenoma which will turn out, on final analysis, to be some other condition. I have had that experience; I think it occurred the day my associates and I began the treatment of pituitary adenoma. I treated my first

patient with a condition diagnosed as such in 1920; in that case the disturbance proved to be internal hydrocephalus of the third ventricle; the diagnosis had even been verified by operation, at which a cystlike structure was observed, said to be the wall of a cyst. We narrowly escaped never learning the true diagnosis, for after the neurosurgeon had told us that the diagnosis was correct and that the tumor we had described in the pituitary fossa was there, though it proved to be cystic, we naturally considered the diagnosis to be verified. I wish to point out that the diagnosis may be at fault; I shall go so far as to say that in a series of 40 or 50 cases in which no operation is performed there will be errors in diagnosis, judging from past experience. Dr. Edward Bancroft Towne (Roentgen-Ray Therapy of Pituitary Tumors, ARCH. NEUROL. & PSYCHIAT. **15**:92 [Jan.] 1926) reported on a series of patients whom I treated from 1922 to 1926; it is interesting that as long ago as that the figures were about the same as those reported today, and from what Dr. Dyke told of his technic, the method used then was not much different.

I wish to enter a plea for study of the technic in this condition. Few will ever have the opportunity that Dr. Dyke and Dr. Hare have had to study a large series; it interests me that the histologic picture in this condition resembles closely that in certain tumors which in my experience have reacted more favorably to spacing between doses of from one to three weeks than to a dosage similar to that used in carcinoma of the larynx, for example, in which I believe the best results are obtained by treating the patients every day. It makes a great deal of difference what interval is used between the exposures. One would expect a quite different action and result with a certain dose repeated at weekly intervals than with the same dose given at an interval of one day; I believe that the field is one which is open to study, and that Dr. Dyke can do the work better than some who have fewer cases of pituitary adenoma a year. Even in this series it would be difficult to evaluate the time factor; yet there are theoretical reasons for believing that one might find it of advantage to maintain the same dosage per field and per exposure that he is using but to try a greater interval between exposures.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, April 15, 1937

FRANCIS J. GERTY, M.D., *President, in the Chair*

GUNSHOT WOUND OF THE HEAD: REPORT OF A CASE. DR. HAROLD C. VORIS.

History.—A girl aged 3 years, who was referred to me by Dr. Herbert Landes on Aug. 22, 1934, nine days previously had been accidentally shot in the head with a 0.22 inch caliber revolver, the bullet passing first through the side of a heavy box and then striking her in the right occipital region. She had been hospitalized immediately and had been delirious and restless during the next two days. The parents insisted that there had been no apparent paralysis until two days after the injury, when complete paralysis of the left extremities appeared. She was kept in the hospital for a week and then brought to Chicago.

Examination.—The child was well developed; she was slightly stuporous but was very irritable when aroused. There was a small, partially healed wound in the posterior occipital region on the right, slightly superior to the mastoid process. General physical examination gave otherwise essentially normal findings.

Neurologic examination showed that the pupils were widely dilated and equal and did not react to light. On the left side there were complete paralysis of the extremities, with increase of the tendon reflexes, absence of abdominal reflexes, and a positive Babinski sign. There was partial paralysis of the muscles of the lower part of the left side of the face. It was not possible to determine whether

any defects were present in the visual fields. Sensory examination was also unsatisfactory, but there seemed to be impairment of pain sensibility on the left side of the body, especially in the upper extremity.

Spinal puncture performed on the following day, with the child struggling, revealed slightly xanthochromic fluid, which contained 5 lymphocytes per cubic millimeter. The pressure was moderately increased.

Course.—The child's general condition improved during the next week, and the stupor and irritability disappeared. A posterior splint was applied to the left leg and foot to prevent foot drop, and she was allowed to go home. There had been no change in the neurologic findings at the time of dismissal.

The patient was seen again sixteen days later. She was then able to raise the left leg and arm and to take a few steps with support. The mother stated that the first movement in the leg had occurred a week after dismissal from the hospital. She was advised to discard the splint, to continue with passive movements of the left arm and leg and to encourage active movements as much as possible. When seen again a month later, the child was able to walk with assistance and to take a few steps alone. She could squeeze objects slightly with her left hand and raise her left arm to the level of the shoulder.

Three months after the injury she was able to walk alone, with a typically hemiplegic gait. She could raise the left arm above the head. Moderate atrophy of the muscles of the extremities on the left side was noted.

Six months after the injury she was walking well and had learned to ride a tricycle. The deep reflexes were markedly increased on the left side. There was little spasticity in the lower extremity but considerable in the upper; voluntary dorsiflexion of the wrist was poor. It was recommended that a "cock-up" splint be applied to the left hand at night.

A month later dorsiflexion of the wrist was much improved, and the grasp reflex was less pronounced. There was slight pes planus of the left foot, and an orthopedic heel and special exercises for the foot were advised.

On Nov. 10, 1936, over two years after the injury, function of the left hand was considerably improved. Plantar flexion of the left foot was carried out well, but dorsiflexion was weak. Supination of the left forearm was difficult. There was no drooping of the shoulder or curvature of the spine.

I did not attempt to remove the bullet, for it seemed not to be doing any harm in its location, as shown by roentgenography a week after the injury; it appeared better to leave it alone than to exchange the risk of cerebral damage from operative trauma for any theoretical improvement that might result from removal.

EXPERIENCES WITH INSULIN SHOCK THERAPY IN SCHIZOPHRENIA. DR. HANS H. REESE, Madison, Wis., and DR. ADRIAN VANDER VEER, Albany, N. Y.

The histologic and physicochemical alterations in insulin shock are given. The electrocardiogram reveals only temporary flattening of the T wave. Conditions of recent onset only are suitable for this new treatment; if the disease has been manifest for more than eighteen months the chance for permanent improvement is slight. Disease of the coronary arteries and severe pulmonary or cardiac disorders are contraindications to treatment; we do not treat patients over 40.

We employ a modified version of Sakel's original regimen. We begin with a dose of 60 units of insulin on the first day, given intramuscularly at 7 a. m. This amount is increased daily by from 10 to 20 units until deep coma is produced. Treatment is given once each week-day. If no improvement is evident after a trial of two months, therapy is discontinued. As sensitivity to insulin appears, as shown by the progressively earlier advent of coma each day, the shock dose must be gradually reduced, sometimes to one fifth of the original amount.

We have noted three types of shock. Wet shock, with profuse sweating, somnolence, ataxia, dysarthria and coma, is the most desirable reaction. "Dry shock" is the term used to describe coma without sweating; we have had some success in converting this undesirable reaction into wet shock by the use of pilocarpine hydrochloride, in doses of from $\frac{1}{10}$ to $\frac{1}{5}$ grain (6.5 to 12.9 mg.). Epilepti-

form shock, in which severe convulsions appear, usually requires prompt termination with intravenous injection of dextrose. Pathologic reflexes and sometimes various decerebrate phenomena are seen in insulin coma. Extreme degrees of psychomotor excitement sometimes precede the advent of coma.

We usually allow quiet coma to continue for from two to three hours, provided the total period of hypoglycemia does not last over seven hours. Complications which may require earlier termination are: weak or irregular pulse, tachycardia with a rate of over 150, respiration of the Cheyne-Stokes type, cyanosis pallor, glottic spasm, hyperpnea, convulsions, excessive salivation (with aspiration), prolonged extensor spasms and hunger and thirst excitement.

Of the four methods used for terminating shock we have found three to be satisfactory: giving carbohydrate by mouth (if the patient is conscious), administration of carbohydrate by nasal tube and intravenous injection of dextrose, in amounts of from 5 to 15 Gm. We have had no success with giving epinephrine alone by any route.

Consideration of the mortality figures from Europe (1.5 per cent of deaths in 395 cases) demonstrates that the dangers of insulin shock therapy have been exaggerated. We have encountered numerous complications, however, which demand careful handling. Among them are: (1) persistent vomiting; (2) aftershock; (3) sialorrhea; (4) hunger and thirst excitement; (5) hypertonic extensor spasms; (6) sensitivity to insulin; (7) elevations in temperature; (8) difficult arousal, and (9) convulsions. The unknown elements in insulin treatment are illustrated by the appearance of convulsions after adequate carbohydrate intake. There is now experimental evidence that hypoglycemic convulsions depend on the degree of hydration of the organism.

No adequate theory to explain the success of insulin shock therapy has yet been advanced. We have treated 21 patients up to the present, with both good results and complete failure. We dare not be too optimistic until the test of time has been applied to remissions that have been observed.

DISCUSSION

DR. PAUL C. BUCY: There has been considerable question in the past as to whether dextrose administered by rectum in man is absorbed at all, or in sufficient quantities to be of value to the organism. These states of hypoglycemia would seem to present an excellent opportunity to determine this point. Has Dr. Vander Veer made any observations as to the efficiency of administering dextrose in this manner?

DR. ALFRED P. SOLOMON: I have observed that improvement does not take place in psychotic patients when they are subjected to hyperinsulin reactions. It has been my experience at the Psychiatric Institute of the University of Illinois College of Medicine that often it is difficult to make a diagnosis of schizophrenia in the first six months of the disease. I refer to conditions often classified in the motley group of dementia praecox which are sharply determined psychogenically, do not exhibit the progressive exacerbation of the disease with characteristic clinical manifestations and sometimes remit spontaneously. It is conceivable that patients in such a passive narcissistic state would welcome the opportunities for masochism offered in these severe treatments and would thus obtain remissions. I have observed a singular lack of protest in some of these patients to the later and more severe treatments of the extended course.

I have thought that this type of treatment offers a rare opportunity to differentiate the clinical types of dementia praecox. It is only by careful psychologic study of such patients when under treatment that one can evaluate the results.

DR. I. R. SONENTHAL: Treatment of patients at the Psychiatric Institute began in November 1936, with 4 patients, and 7 patients are under treatment at present. One of this series of 11 patients had disease of recent onset—of three months' duration. The others had been ill for from one to seven years—7 for from one to one and a half years. Of this group 2 have a paranoid type of dementia

praecox; 5, a hebephrenic form, and 2, a catatonic. One has atypical manic-depressive psychosis and the other dementia simplex.

The lowest level of the blood sugar that has been reached in the depth of coma is 15 mg. per hundred cubic centimeters. In 1 case the blood pressure rose from 40 to 70 mm. of mercury. Phase I lasted from six to eighteen days in the first 4 patients treated. Phase II consisted of from eight to thirty-five shocks, in which coma lasted from five minutes to two hours and twenty minutes. The average dose which produced coma in the 4 patients was 120, 135, 160 and 175 units, respectively.

Although Sakel urged that no psychologic exploration should be made after treatment, we believe that recovery may be judged by the amount of insight exhibited. Insight is tested by having the patient reproduce in what ways his behavior and ideas compare with those shown on his admission.

In discussing the results, my associates and I hesitate to make optimistic statements. Two of the first 4 patients treated are still in the ward and are unimproved. We agree with Dr. Vander Veer that though this therapy promises to be encouraging in dementia praecox, enough cases have not been observed for at least five years to permit proper evaluation. It is not unexpected to learn that observers in Vienna obtained their highest rate of remission (from 70 to 80 per cent) in conditions of recent onset.

This applies also to the paranoid type of dementia praecox, which is known to be peculiarly unyielding to other types of therapy. The question then arises as to the contradiction in calling the paranoid form of dementia praecox recent. It is well known that this condition is insidious in onset and does not become apparent for several years.

I wish to ask Dr. Vander Veer what are his criteria for judging the stage of coma. What are the indications for interrupting coma?

DR. CHARLES F. READ, Elgin, Ill.: The paper presented reports much the experience which my associates and I have had thus far at the Elgin State Hospital, but I should not attempt at this time to present any statement as to our results. The number of cases, 13 thus far, is too small, and the patients have been under treatment only ten weeks.

I am much interested in this form of therapy, in view of another treatment that has become popular recently—Meduna's therapy with metrazol, which produces prompt epileptiform seizures after injection of the drug into a vein. We have checked on Meduna's therapy in a few cases and have had some startling results thus far. If this method produces good effects—and the statistics are almost the same as those for insulin shock therapy—one might attempt to relate insulin therapy to the production of epileptiform seizures for curative purposes. I have obtained the impression, in looking at a number of patients in hypoglycemic shock, that one is witnessing atypical status epilepticus. There are many similarities. In a recent article by Dr. Paul I. Yakovlev (Neurologic Manifestations Concerned in Epileptic Seizures, ARCH. NEUROL. & PSYCHIAT. **37**:523 [March] 1937) there is a critical study of epilepsy. If one observes patients in hypoglycemic shock, one will be struck with the similarity in the procedure of the shock, as exhibited in patients at various times, and the progress of an epileptic convulsion —with coma, dystonic movements, vagotonic states alternating irregularly with sympathetic effects, evidences of decerebrate rigidity, as mentioned in the aforementioned paper, and various neurologic findings. I wonder whether in both these treatments one is not producing a similar effect on the central nervous system, whatever that may be. Possibly one is producing a change in the physiologic reactions of the brain, which may be "wild," as it were, but which are afterward overcompensated for, with consequent return to the normal status in many patients.

DR. ARTHUR WEIL: In 1936 I had the opportunity to study the insulin shock therapy at Münsingen, Switzerland, and at Vienna. I wish to point out a problem which was not mentioned in the present paper but which was discussed frequently in European clinics. It was the question how long a patient should be treated

with insulin shock before the therapy is given up as hopeless. After pooling the experiences of the Swiss, Austrian and Polish clinics, it was decided at Professor Pötzl's clinic, in Vienna, that at least fifty shocks should be obtained before the patient should be considered incurable by this method.

DR. ADRIAN VANDER VEER: In reply to Dr. Bucy: I regret that we have not tried the administration of dextrose by rectum.

As to Dr. Solomon's discussion: I may say that we have not had much trouble in classification—perhaps because we are dealing not with ambulatory patients but with state hospital material and such patients usually present a fairly typical condition. In so far as questionable diagnoses may affect the validity of our results, I may say that in only 2 of our cases was the disease atypical, presenting little more than marked "hypertrophy of the ego" and preoccupation with meaningless philosophic problems. It is interesting that we had practically no success with them.

Dr. Sonenthal mentioned Sakel's dictum that there should be no deep psychologic exploration in these cases. We believe that this holds true during treatment but that on discharge the patients should be subjected to as thorough an examination as one can conduct, in order to estimate the degree of healing. As for the criteria by which we estimate the depth of shock: We have evolved and changed them as our experience has increased. We now say that a patient is in light wet shock when he sweats and is perhaps a little dysarthric. We consider him in moderately deep shock from this point until he can no longer execute the simplest commands. When the patient cannot so respond we class him as comatose, though he may still react reflexly and even swallow liquids.

We, too, have had interesting experiences with Meduna's convulsive therapy, as has Dr. Read. In a young woman with catatonic stupor we induced complete remission, with full insight, after only two convulsions (three days of treatment). I do not believe, however, that there is much in common between the symptomatology of typical epileptiform convulsions and that of deep insulin shock. It is hard to find any similarity between wet shock, in which the patient is quiet and relaxed, and a true epileptiform fit. Certainly, many of the myoclonic reactions under insulin bear a superficial resemblance to epileptiform phenomena; but as our experience has increased, we have differentiated more sharply between myoclonic responses and real epileptiform attacks.

We believe with Dr. Weil that a patient should receive a minimum of three months' treatment, or fifty shocks, before he is dismissed as hopeless. From practical considerations, however, we have shortened this period of trial to about two months. We would try longer, for occasional patients respond favorably only later, but lack in space and staff at present compel us to adhere to this time limit. Under our present conditions of work we feel able to treat with safety no more than 11 patients at one time.

HUNTINGTON'S CHOREA: A GENEALOGICAL STUDY. DR. THEODORE T. STONE and DR. EUGENE I. FALSTEIN, Elgin, Ill.

Fifty-two patients with Huntington's chorea admitted to the Elgin State Hospital since 1900 were studied genealogically; 10 families are described in detail, representing more than half the patients with a family history of the disease. The nationalities represented by the patients in the Elgin State Hospital and other state hospitals in Illinois include German, English, Scotch, Irish, Slavonic, Scandinavian, Lithuanian, Italian, Jewish, and Negro groups, with many mixtures as well. There is a surprising prevalence of chorea among Germans.

About four times as many patients are admitted from urban as from rural districts. The incidence based on age, as far as onset of symptoms is concerned, includes every decade to the ninth, except the first, with the largest number of cases occurring in the fifth.

Equal numbers of male and female patients with chorea have been admitted to the Elgin State Hospital; for the state of Illinois as a whole it appears that more female than male patients have been admitted, though the difference is not

great. Various biotypes of chorea are observed, each with some dissimilar symptom; in some families the disease comes on relatively early and in some late; in some the mental symptoms precede the choreiform movements, while in others the latter initiate the disturbance.

Anticipation occurs but is not a constant characteristic of the disease; on the contrary, it appears to be the exception and is to be expected usually when neuropathic stocks are interbred.

The most reliable histories reveal a typical mendelian dominance.

As regards the disorder as a social and eugenic problem: At present, about three hundred years after its introduction to America and sixty-five years after Huntington's treatise was published, the disease appears to be out of control and challenges mental and social hygiene movements. Prospects of its eradication appear to be remote without adequate legislative measures of the type exemplified by legalized sterilization.

DISCUSSION

DR. FRANCIS J. GERTY: Were any members of the family reported by Dr. A. S. Hamilton, of St. Paul, included in this series? Three of that family have been patients in the Cook County Psychopathic Hospital. Hamilton published in the *American Journal of Insanity* (**64**:403, 1907-1908) the history of this family, covering five generations; I wonder whether any of these patients were included.

DR. CHARLES F. READ, Elgin, Ill.: I am not fitted to discuss this paper in detail, but it represents considerable clinical work; Huntington's original paper was also purely clinical and emphasizes that many good papers may be presented without an extensive laboratory work-up. Eighty-six cases of this disease are recorded in Illinois. If the descendants of the patients could be followed for the next one hundred and fifty years it would probably be found that they would give rise to many other choreic patients, thus involving a host of economic and social difficulties. It would seem that cases of familial degenerative disease of this type, as well as others, should be reported and that the children of these ascendants should be sterilized at an early age, to prevent extension of the disease. It is distressing to note that one of these patients has six siblings still alive who may disseminate the disease further.

DR. SIDNEY D. WILGUS, Rockford, Ill.: I remember the case at the Elgin State Hospital reported in 1910 which was mentioned in this paper; I believe that the mother had the same trouble. In Rockford one occasionally sees patients with this disease in the general population.

DR. EUGENE I. FALSTEIN: We included Dr. Hamilton's patients in our studies, but, as far as we know, our patients are not directly related to his. We intend to trace the patients further, however, and in that connection we shall be glad to make use of Dr. Wilgus' observations.

I wish to thank Dr. Read for his discussion and, in closing, to add that this paper is one of a series dealing with the various aspects of Huntington's chorea.

RELATIONSHIPS OF OXYGEN AND CARBON DIOXIDE IN THE BLOOD OF PATIENTS WITH CONVULSIONS. LOREN W. AVERY.

Book Reviews

The Psychology of Adjustment: An Objective Approach to Mental Hygiene. By Laurance Frederic Shaffer, Ph.D., Associate Professor of Psychology, Carnegie Institute of Technology. Cloth. Price, $3. Pp. 600, with 26 illustrations. Boston: Houghton Mifflin Company, 1936.

Written in a lucid, simple style and intended for the general college student, "The Psychology of Adjustment" may also be read with profit by many physicians in the psychiatric field of clinical practice. It presents the advances in psychology of the last ten years in a convenient, concise form and reviews fundamentals in a field which may have been adjudged in the past as affording inadequate help in clinical problems. The book will also be useful as a text in courses in human behavior for medical students. As such a text, it will be of assistance to those interested in the improvement of undergraduate instruction in a psychiatric approach not only to the problems of frank, classifiable psychoneuroses but to the behavior disorders of children and the emotional difficulties of patients with somatic diseases. For this purpose the division of the book into four parts, dealing with "Psychological Foundations," "Varieties of Adjustive Behavior," "Personality" and "Technique of Mental Hygiene," is fairly well adapted, although the order in which the material is presented might be somewhat altered. Thus, in a general preparatory course for freshmen and sophomores the first and third sections seem more suitable. These sections treat such elementary topics as "The Origins and Modification of Behavior," "Motivation," "Adjustment," "Personality Traits and Their Measurement" and "Organic Factors in Personality." The last chapter in the third section, entitled "The Development of Personality Traits," in which maldevelopments are also discussed, appears, on the other hand, to be more closely related to the field of maladjusted behavior and therefore to a course during the junior year. In this course the material of the second and fourth sections could well be combined with the demonstration of patients to exemplify forms of adjustment which benefit from clinical attention and to illustrate methods of therapy. The second section ("Varieties of Adjustive Behavior"), which is divided into such chapters as "Adjustment by Defense," "Adjustment by Ailment" and "Persistent Non-Adjustive Reactions," presents a logical development of the fundamental principles of the first section, describing simply and objectively the phenomena of clinical importance. In order to give some attention to the problems of therapy, the material of the last section might also be included. Even as collateral reading in clerkships or dispensary courses of the senior year, perhaps particularly in pediatrics, as well as in psychiatry, the last three chapters, entitled "Mental Hygiene Study of the Individual," "Guidance of Readjustment" and "Applications of Positive Mental Hygiene," fill a long-felt need. Only too frequently are the student, the intern and the recent graduate almost entirely unacquainted with the function of the psychologist and the psychiatric social worker, either in child guidance or in an adult psychiatric clinic. This lack of familiarity with the rôle of specially trained personnel in such integrated units in fields other than the medical and with the general methods of such clinics leads too often to unnecessary misunderstanding and inadequate cooperation.

Appended to each chapter in the book is a list of suggested collateral reading; a series of questions and exercises for discussion of each chapter forms a separate appendix. A table of contents, an index and an extensive bibliography add considerably to the usefulness of the text. Following the third section, a chapter dealing with the critical evaluation of psychoanalysis lends itself well to orienting the student to the relation of this school of thought to clinical medicine and psychiatry and supports editor Carmichael's statement in the introduction that "scientific psychology has come of age." As he puts it, "The student well trained in mathematics, physics, chemistry, biology and scientific psychology is often rightly repelled by the books on personality, mental hygiene, clinical psychology and abnormal psychology which he reads. He has been trained to respect measurement and the scientific method, and he is given anecdotes and stories from mythology." With this the present reviewer is in complete agreement, and he believes that Shaffer's book is a stimulating and much needed contribution to the literature.